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INTENSIVE STUDY OF FIFTY CASES OF NEURO-CIRCULATORY ASTHENIA

REPORT ON FIFTY CASES OF SO-CALLED CONSTITUTIONAL NEURO-CIRCULATORY ASTHENIA *

ALFRED FRIEDLANDER, M.D. (CINCINNATI)
Major, M. C., U. S. Army, Chief of Medical Service, Base Hospital

AND

WILLIAM L. FREYHOF, M.D. (CINCINNATI)
Captain, M. C., U. S. Army, Cardiovascular Specialist, Base Hospital

CAMP SHERMAN, OHIO

With the recognition of a cardiac class for remediable military recruits after the elimination of the unquestionably unfit, the so-called constitutional cardiac neurotic presents an extremely difficult problem. We have attempted to study intensively fifty such cases taken from all varieties of military service-men deemed unfit for overseas duty and who, in contradistinction to the possible infectious and functional group, were selected because of the constitutional or pre-enlistment nature of their complaint. This so-called neurocirculatory asthenic who reports for military duty has not been subjected to the strain of early training, nor has he recently suffered severe infection. He has complained of cardiac distress for years. He is made of poor material that has been constantly irritated. His start in life is only fair at best, and therefore, with added external and internal irritation he becomes a poorly disciplined waster of nervous energy.

This group is particularly susceptible to external stimuli. These men have allowed themselves to spend their nervous energy so recklessly that they are constantly on the threshold of stimulation and any slight irritation, emotional or otherwise, pushes them over the border and they respond as recklessly as they have always been accustomed to. With this point in view we have not considered this condition a definite clinical entity. It just so happened that in the

* Submitted for publication Aug. 13, 1918.

business of sorting, these cardiac neurotics were grouped together. Knowing the external stimuli, an investigation was attempted to find and remove all foci of irritation of an internal nature. At the same time a system of exercise was adopted in which men passed from mild to higher grade exercises in conjunction with route marches of one to six miles with and without light and full pack. Five groups were established, and after three days the man was moved to a higher grade exercise under favorable circumstances along with games and competitive drills. At the outset it was impressed on the men that they were not patients, but men under strict military discipline. A competent drill sergeant lived with the men and became both their leader and adviser. Competition and special privileges, along with a certain amount of pride in the police of their barracks, soon brought out the best that was in them. With the men satisfied with their surroundings, doing work and playing games within their limit of tolerance, all external stimuli were easily controlled. At the same time the internal stimuli or foci of irritation were rigidly investigated. The accompanying tables attempt to analyze this situation, and prove that there are definite foci which tend to lower the man's nerve capital and increase the offensive force to a point far above his defensive. With graduated exercise and discipline we hope to build up this defensive force and eliminate the offensive by removal of all irritating foci both internal and external.

The following schedules present the plan of procedure and take a typical case through the entire course. The tables present summaries of our study of fifty cases of so-called neurocirculatory asthenia. We have attempted to analyze these cases after the method of Thomas Lewis[1] of England.

At present no attempt is made to draw sweeping conclusions from these studies, which are herewith presented as a preliminary contribution to the subject.

Past History—Prevalence of Past Infection.—Measles, whooping cough and tonsillitis seem to have played the greatest rôles in the past history of the cases under observation. Gonorrhea, pneumonia, scarlet fever, rheumatic arthritis and typhoid are next in frequency, and it is to this group of diseases that 22 per cent. of the patients date the onset of their present condition.

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1. Report of Medical Research Committee, Series No. 8. Reports on Soldiers Returned as Cases of "Disordered Action of the Heart" (D. A. H.) or "Valvular Disease of the Heart" (V. D. H.).

TABLE 1.—Typical Case Record

CARDIOVASCULAR CASE RECORD NO. ....

Name, X Y Z Rank, Pvt. Co. .... Regt. .....Inf.
Age, 22 years. Race, White. Service (Yrs., 8/12)
Occupation, Farmer
Invalided, In training

History.—Family—Maternal uncle T. B.—Mother very nervous—Grandfather, cancer.
Past—Measles, pertussis.
Habits—No. cigarets 4. Cigars 2. Pipes 0. Chews 3. Alcohol moderate.
Onset—Gradual, cause unknown.
Symptoms—Duration, 4 yrs. No. Repetitions, Three times. Dyspnea, Yes. Pain, Yes. Palpitation, Yes. Fainting, No. Giddiness, Yes. Sweating, No. Flushing, No. Cough, No. Weakness, No. Nervousness, Yes.

Thyroid Gland—Tumor, No. Tremor, Yes. Exophthalmos, No. Diarrhea, No.

Cardiac Status on Admission:
Thrills—None
Apex Impulse—5th Space 9.0 cm. M.L.
Borders—R. 3d Space 3.0 cm. M.L.
L. 5th Space 10.5 cm. M.L.
Sounds—Base, P 2 = A 2
Apex, Clear
Murmurs—Apex, None
Base, None
Exercise Test:
Standing Rate 144
Recumbent Rate 126
Rec. after Ex. Rate 150
Rec. 2 min. Rate 132
Arrhythmia—Respiratory
Bld. Pr.—Systolic 144, diastolic 95

Cardiac Status on Discharge:
Thrills—None
Apex Impulse—5th Space 9.0 cm. M.L.
Borders—R. 3d Space 3.0 cm. M.L.
L. 5th Space 10.0 cm. M.L.
Sounds—Base, Clear
Apex, Impure 1st apical
Murmurs—Apex, None
Base, None
Exercise Test:
Standing Rate 84
Recumbent Rate 84
Rec. after Ex. Rate 96
Rec. 2 min. Rate 84
Arrhythmia—Respiratory
Bld. Pr.—Systolic 136, diastolic 84

Group Progress—Good; highest grade exercises well tolerated
Weight, 6 Day Intervals—149, 154, 156, 154, 158, 154, 159, 154
Date of Admission—5/15/18 Discharge—7/15/18 Observation Time—62 days
Final Disposition—Unrestricted military duty
Diagnosis—Neurocirculatory asthenia, constitutional

TABLE 2.—Typical Case Record

CASE RECORD NO. ....

Name—X Y Z Rank—Pvt. Co. — Regt. —— Inf.

General Physical	Cardiac	Psychiatric
General Appearance — Erect; well developed and tanned; dermatographia. Lungs—Clear Abdomen—Negative Extremities—No cyanosis; hands clammy	R. C. D.—Within limits Sounds—P 2 = A 2 Murmurs—None Exercise—Response fair Action—Rapid, regular	Negative Mental Age—Adult

Neurological	Ear—Nose—Throat	Dental
K. K.—Coarse tremor of tongue; hands extended	Ears—Negative Nose—Nasal spur Lt. Throat—Tonsils hyper. bilateral 2 x; pus present Trans.—Negative Diag.—Tonsillitis, chronic, suppurative	R-14, Dental alveolar abscess. Indication for extraction. Incomplete D. A. A.—R-14 extracted. Conductive anesthesia

Gastro-Enterological	Genito-Urinary	X-Ray
History—Physical examination, stool and stomach analysis, negative	Prostate—Normal	R. U. 2.0 L. U. 3.0 L. M. 5.5 R. L. 4.0 L. L. 10.0 Gastro-Intestinal—Negative

Laboratory

Blood	Urine	Stool
Hemoglobin—70% Red—7,184,000 White—6,600 Differential—Not indicated	Color—Light straw Appearance—Clear Reaction—Acid Sp. Gr.—1.022 Albumin—Negative Sugar—Negative Microscopic—Negative	Color—Dark brown Consistence—Solid Mucus—Negative Blood—Negative Microscopic—Negative

Wassermann—Negative Prostatic Smear—Negative

TABLE 3.—Reconstruction Schedules

U. S. ARMY BASE HOSPITAL, CAMP SHERMAN, OHIO

Daily Schedule for "Reconstruction" Hospital

A. M.	6:00	First call
	6:20	Fully dressed, police around ward
	7:30	Breakfast, mop floors and clean up details
	8:00	Exercises
	9:00	Physical examinations, review marching order
	11:00	Absolute rest on beds
	12:30	Mess
P. M.	1:00	Recreation
	2:00	Exercises and route marches
	3:00	Games
	4:00	Police and clean up
	5:00	Mess
	6:15	Retreat
	9:00	Taps—All lights out.

Schedule of Exercises Cardiovascular Reconstruction

	Exercise	Time	Days
Group 1	1	15 min.	3
	1A	20 min.	3
Group 2	2	15 min.	3
	2A	20 min.	3
Group 3	3	15 min.	3
	3A	30 min.	3
Group 4	3A and 1	30 min. at 1 mile	3
	3A and 2	30 min. at 2 miles	3
	3A and 3	30 min. at 3 miles	3
	3A and 4	30 min. at 4 miles	3
	3A and 5	30 min. at 5 miles	3
	3A and 6	30 min. at 6 miles	3 without pack
Group 5	3A and 7	30 min. at 6 miles	3 with light pack
	3A and 8	30 min. at 6 miles	3 with full pack
			Total 42 days

TABLE 4.—Reconstruction Schedules

U. S. ARMY BASE HOSPITAL, CAMP SHERMAN, OHIO

Graduated Exercises of Cardiovascular Reconstruction

Exercise 1

Position	Exercise	Command	Count
Arms to thrust, raise	Raise and lower shoulders	Up, down	15 times
Arms to thrust, raise	Shoulders back and forward	Front, back	15 times
Hands clasped back head	Head forward and back	Front, back	15 times
Hands on hips, place	Head twist, left and right	Left, right	10 times
Arms extended, raise	Clinch and open fist	1, 2	20 times
Arms extended, raise	Describe circles palms up	Back, front	1 min.
Arms backward, cross	Quarter bend knee	1, 2	15 times
Attention	Breathing exercise, inhale and exhale	Arms forward, up, back, downward	10 times

Exercise 2

Hands on shoulders, place	Thrust arms forward, sideward and upward	1, 2, 3, 4	10 times each
Arms backward, cross	Quarter bend forward	1, 2	10 times
Hands clasped back head	Head forward and backward	Front, back	15 times
Hands on hips, place	Raise on toes	1, 2	15 times
Hands on hips, place	Extend leg forward, ankle high and knee high. L. and R.	1, 2, 3, 4	15 times each
Hands on hips, place	Raise leg sideward. L. and R.	1, 2, 3, 4	10 times each
Arms extended, raise	Describe circles	Back, front	1 min.
Hands on hips, place	Raise knee to level. L. and R.	1, 2, 3, 4	15 times
Attention	Breathing exercise, inhale and exhale	Arms forward, up, back, downward	10 times

Exercise 3

Hands on shoulders, place	Arms forward, upward, sideward	Front, up, down	20 times each
Hands on hips, place	Full knee bend	1, 2	8 times
Hands on hips, place	Bow oblique to L. and R.	1, 2, 3, 4	10 times
Hands on hips, place	Bend trunk backward	1, 2	10 times
Hands over head, raise	Bend and touch toes	1, 2	8 times
Arms to thrust, raise	Step and strike obliquely to left and right	1, 2, 3, 4	15 times
Arms on hips, place	Extend leg forward, ankle high and waist high. L. and R.	1, 2, 3, 4	10 times each
Hands on hips, place	Rotate head L B R	1, 2, 3, 4	10 times
Attention	Breathing exercise, inhale and exhale	Arms forward, up, back, downward	10 times

TABLE 5.—Past Infections

	No.	Per Cent.		No.	Per Cent.
Measles	46	92	Rheumatic arthritis	7	14
Pertussis	35	70	Typhoid	7	14
Tonsillitis	30	60	Diphtheria	4	8
Gonorrhea	13	26	Malaria	3	6
Pneumonia	12	24	Mumps	2	4
Scarlet fever	11	22	Meningitis epidemic	1	2

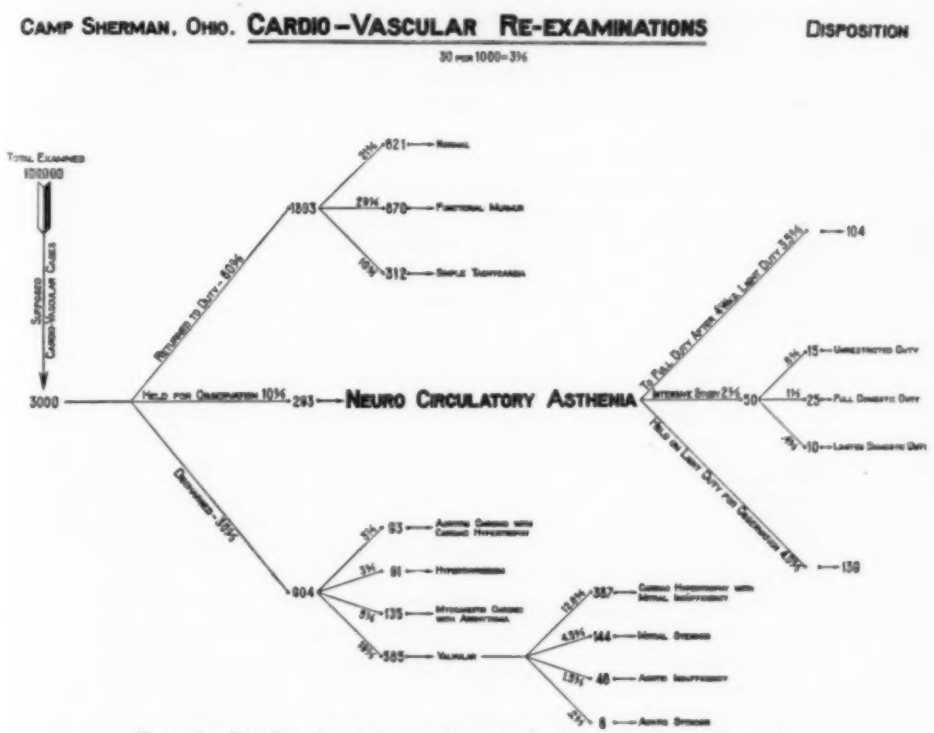

Chart 1.—Results of cardiovascular examinations at Camp Sherman.

Present Condition—Prevalence of Symptoms.—Pain was the most frequent symptom complained of. The location of the pain was usually in the precordial region; at times in a well defined area, but again seemed to be a hyperalgesia of the chest wall. Dyspnea on exertion, paroxysmal palpitation, giddiness, nervousness, weakness, sweating and flushing were next in order of frequency of occurrence. *No one symptom predominated.* Precordial distress including dyspnea, pain and palpitation, nervousness, weakness and giddiness characterize the syndrome.

TABLE 6.—Present Symptoms

	No.	Per Cent.		No.	Per Cent.
Precordial pain	44	88	Nervousness	22	44
Dyspnea	40	80	Weakness	22	44
Palpitation	37	64	Flushing	16	32
Giddiness	27	54	Fainting	5	10
Sweating	27	54	Cough	4	8

Previous Occupation—Civilian Life.—A large portion of this class is drawn from those having sedentary or light occupations. Forty per cent. of the group under study belong to this class. This percentage might even be increased to 53 per cent., since we list 13 per cent. as farmers who call themselves such merely because they live on a farm and do light work.

TABLE 7.—Previous Occupations of Fifty Patients

	No.	Per Cent.		No.	Per Cent.
Farmer—light work only	13	26	Engineer—stationary	1	2
Clerks	12	24	Engineer—civil	1	2
Mechanics	4	8	Attorney	1	2
Carpenters	3	6	Contractor	1	2
Electricians	2	4	Merchant	1	2
Illustrators	2	4	Jeweler	1	2
Coal miners	2	4	Optician	1	2
Laborers—common	2	4	Barber	1	2
Printer	1	2	Bartender	1	2

TABLE 8.—Military Service when Invalided (Fifty Patients)

	No.	Per Cent.		No.	Per Cent.
Infantry	35	70	Artillery—heavy	2	4
Machine gun	7	14	Signal—field	2	4
Quartermaster	2	4	Engineers	2	4

Onset of Symptoms.—The patients' statements as to onset, cause and duration of symptoms are rather indefinite. Twenty-two per cent. gave a history of a sudden onset and these dated their condition from some previous illness, although this entire group had been more or less nervous and below par since childhood. In 78 per cent. the onset was gradual and the majority of these could give no definite reason or cause for their present condition. In most cases repetition of symptoms occurred with exercise, many others were due to emotional disturbances, and the remainder persisted constantly.

TABLE 9.—Occurrence of Symptoms

	No.	Per Cent.		No.	Per Cent.
Onset—sudden	11	22	Ascribed Cause of Onset—Patients' Statements:		
Onset—gradual	39	78			
Repetition—with exercise	25	50	Malaria	1	2
Repetition—with emotion	10	20	Railroad accident	1	2
Repetition—constant	15	30	LaGrippe	2	4
Ascribed Cause of Onset—Patients' Statements:			Typhoid	2	4
			Pneumonia	2	4
Cause unknown	31	62	Scarlet fever	1	2
Overwork—sudden strain	5	10	Gonorrhea	1	2
Overtrained	2	4	Bronchitis	1	2
Overheated	1	2			

Duration of Symptoms.—Forty-seven out of the fifty cases under observation gave a history of nervousness and cardiac distress previous to induction into military service. Development of symptoms followed scarlet fever in one case and the severe strain of overtraining in two cases.

TABLE 10.—Duration of Symptoms and Years of Service

Average Duration of Symptoms

Years	No.	Per Cent.	Years	No.	Per Cent.
20	2	4	6	6	12
18	1	2	5	5	10
16	2	4	4	4	8
13	1	2	3	11	22
10	6	12	2	3	6
9	1	2	1	1	2
8	2	4	1/4	1	2
7	2	4	1/12	2	4

Average Years Service when Invalided

Years	No.	Per Cent.	Years	No.	Per Cent.
9/12	2	4	4/12	1	2
8/12	14	28	3/12	2	4
7/12	8	16	2/12	8	16
6/12	1	2	1/12	13	26
5/12	1	2			

General Physical Status.—The majority of this group showed vasomotor instability as evidenced by alternating flushing, pallor, cold, cyanotic, clammy extremities and marked evidence of dermatographia. Fifty-two per cent. were robust and well developed, while 40 per cent. were rather slender, flat-chested and showed poor muscular tone. One man had a right side empyema following pneumonia. Examination of the lungs showed no evidence of structural change.

TABLE 11.—General Physical Status

	No.	Per Cent.		No.	Per Cent.
Well developed	26	52	Lungs—empyema scar	1	2
Poorly developed	20	40	Congenital asymmetry (face)	1	2
Dermatographia	40	80	Cyanotic extremities (clammy)	40	80

Cardiac Status.—No one in the entire group presented evidence of structural cardiac change. The relative cardiac dulness was constantly within normal limits. Twenty-two per cent. had functional apical murmurs, while 28 per cent. had accidental pulmonic systolic murmurs. Two men showed impure first apical sounds, while two had a reduplication of the first sound. The response to exercise was fair in 40 per cent., good in 50 per cent. and poor in 10 per cent. The exercise test was "One hundred hops on the left foot." Ten per cent. of the men had an apical systolic thrill palpable after exercise or excitement. A respiratory arrhythmia more marked in some than in others was present in all cases.

TABLE 12.—Cardiac Status

	No.	Per Cent.
Relative cardiac dulness within normal limits	50	100
Murmurs: Functional apical systolic	11	22
Accidental pulmonic systolic	14	28
Sounds: Impure first apical	2	4
Reduplication first apical	2	4
P-2 greater than A-2	17	34
A-2 greater than P-2	8	16
Response to Exercise: Fair	20	40
Good	25	50
Poor	5	10
Action: Rapid	44	88
Arrhythmia—respiratory	50	100

Thyroid Status.—Twenty per cent. of the cases under observation presented thyroid tumor to a greater or less degree. This is not unusual appearing in men drawn from the Ohio Valley region. Tremor was present in 96 per cent. of the group, and a mild degree of exophthalmos appeared in 6 per cent. of the cases. History of diarrhea was not elicited. Little importance is attached to these findings as a possible factor of causation of the syndrome under discussion.

TABLE 13.—Thyroid Status

	No.	Per Cent.		No.	Per Cent.
Tumor	10	20	Exophthalmos	3	6
Tremor	48	96	Diarrhea	0	0

Ear, Nose and Throat as Foci of Irritation.—The nose and throat seem to yield the largest number of portals of entry for irritation and infection. Of the group under study the tonsils are the worst offenders, 90 per cent. having chronic suppurative tonsillitis. Thirty-two per cent. of the men showed deviation of the nasal septum, 20 per cent. chronic sinusitis, while 8 per cent. gave evidence of otitis media.

TABLE 14.—Status of Ears, Nose and Throat (Fifty Cases)

	No.	Per Cent.		No.	Per Cent.
Ears: Otitis media, chronic, suppurative	4	8	Sinuses: Chronic sinusitis	10	20
Nose: Deviated septum	16	32	Throat: Tonsillitis, chronic, suppurative	45	90

Teeth and Mouth as Foci of Irritation.—The teeth and mouths of the men under observation showed evidence of recent dental attention; in fact, 66 per cent. of the group presented no evidence of oral infection. Thirty-four per cent. gave positive findings of a degree indicating extraction. Following this procedure and after cleaning up the mouth infection, a definite, marked improvement was observed, not only in general conditions, but a specific beneficial result was noted in the heart rate and character of the response to exercise. This is in accord with the view that systemic irritation results more frequently from nonencapsulated granulomas on the apices of teeth than from definitely encapsulated blind abscesses. All cases under observation show the former condition.

TABLE 15.—Oral Infections (Fifty Cases)

	No.	Per Cent.		No.	Per Cent.
No evidence of oral infection	33	66	Dental alveolar abscess	3	6
Gangrenous pulps	3	6	Carious roots	11	22

Genito-Urinary Status. — All patients under observation denied syphilis, while 24 per cent. (twelve in the group of fifty) admitted gonorrhea. Of the Wassermanns made on all cases, only two (or 4 per cent.) were returned positive (++). These men were immediately subjected to rigid antisyphilitic treatment.

No man presented an active gonorrhea. Rectal examination of the prostate showed 10 per cent. to be soft and slightly enlarged, 10 per cent. moderately enlarged, 6 per cent. small and nodular, the remainder normal. Only one case presented a tender and enlarged right seminal vesicle. Smears made of the expressed secretions following prostatic massage were all negative, no gonococci being demonstrated.

Urine Analysis.—Routine urine examination failed to reveal any unusual findings, the few ordinary tests made being negative. An occasional trace of albumin appeared following heavy marching, but was only of a temporary nature.

Blood Counts.—Average blood counts made on the fifty men showed very little of interest. The average red count was about 5,190,000, white count 8,700, hemoglobin 90 per cent. This ratio persisted through training. Ten cases showing low hemoglobin percentage on admission, after two months forced feeding and graduated exercises showed marked improvement and higher hemoglobin percentage, approaching normal on discharge.

Foci of Irritattion—Psycho-Neurotic Factors. — Psychiatric and neurologic investigations made on the group under observation yielded the data given in Table 16.

TABLE 16.—Psychiatric and Neurologic Data

Family History:	Per Cent.	Personal History:	Per Cent.
Nervousness	72	Previous nervousness	64
Alcoholism	10	Alcoholic excess	4
Insanity	2	Psychasthenia	8
Epilepsy	2	Neurasthenia	4
Tuberculosis	36	Epilepsy	0
Carcinoma	8	Tobacco excess	10
		Head injuries	4

Definite evidence of psychasthenia was obtained in four men, one of whom was a religious fanatic. Two were definite neurasthenics, while four showed positive neurologic findings. The mental age was taken of each case in order that a more definite status might be established. Fifty-six per cent. of this group measured normal adult mentality, while 44 per cent. ranged from 8 to 15 years of age.

TABLE 17.—Comparing Age with Mental Age

Age, Years	Per Cent.	Mental Age*	Per Cent.
33	2	Adult	56
32	2	15	6
31	2	14	6
30	8	12	16
29	6	11	2
28	4	10	6
27	4	9	4
26	12	8	4
25	14		
24	14		
23	12		
22	18		
21	0		
20	2		

* Binet combined point—Yerkes Bridges scale.

In the group under observation it so happened that we were able to study the syndrome under discussion in twins. These men were 22 years of age, well developed and farmers by occupation. The family history showed the mother to be very nervous. The men said they had been nervous since childhood, one dating the onset of symptoms four years, the other sixteen years previously. They served in different regiments and when invalided the one had had three-twelfths year, the other eight-twelfths year training. After completing the course of graduated exercise, both showed marked improvement and were returned to full duty. These two men were not malingering. Indeed, they were most anxious to return to full military duty. Both were of normal mental age, but had since childhood labored under the impression that they were definite "cardiacs." Examination revealed no evidence of structural cardiac change. After cleaning up their very bad mouth and tonsil condition, regulating the diet and graduating their exercise, these men are now rather formidable soldiers, doing full military duty.

Their improvement is shown in the accompanying table (Table 18). Heart and respiratory rates with blood pressure readings were taken before and after treatment.

TABLE 18.—Showing Improvement of Twins on Graduated Exercise*

	Pulse		Respiration		Blood Pressure, Systolic		Blood Pressure, Diastolic		Return to Normal
	Before	After	Before	After	Before	After	Before	After	Minutes
D. C. on admission	108	144	16	18	140	170	90	90	3
D. C. on discharge	80	104	15	16	124	136	84	84	2
D. L. on admission	116	150	16	18	144	160	94	98	3½
D. L. on discharge	80	116	16	17	130	140	90	94	2

* Record of twins aged 22 years. Duration of symptoms 4 and 16 years. Mother very nervous. Exercise used, 100 hops on left foot. Observations made before and after.

Gastro-Intestinal Status.—(Report by Capt. Robert McCaughey.)—The fifty men were asked if they believed themselves to have any stomach or bowel trouble. Forty-four—88 per cent.—answered in the

negative. Six—12 per cent.—made positive declarations. As to past stomach or bowel troubles thirty-eight—76 per cent.—reported negative, twelve—24 per cent.—positive.

Declaration			
Present		Past	
Positive	Negative	Positive	Negative
6.....12%	44.....88%	12.....24%	38.....76%

History and examination showed that twenty-five (50 per cent.) were free from gastro-intestinal irritation, and the same number were found to have definite histories and findings of such trouble. Of these twenty-five positive gastro-intestinal cases, seven (14 per cent.) had intestinal stasis of the atonic type, one (2 per cent.) of the spastic type, and one (2 per cent.) had periodic stasis as shown by the history. Three (6 per cent.) had intestinal stasis associated with gastric atony, nine (18 per cent.) associated with chronic inflammation. Secondary or primary gastric irritation was found in four (8 per cent.) of the group studied.

TABLE 19.—Gastro-Intestinal Status

	No.	Per Cent.
Positive gastro-intestinal cases	25	50
Intestinal Stasis:		
Atonic type	7	14
Spastic type	1	2
Periodic type	1	2
Associated with gastric atony	3	6
Associated with chronic inflammation	9	18
Secondary-primary gastro-intestinal irritation	4	8
Total	25	50

50 cases studied

TABLE 20.—Intestinal Stasis

Number	1	2	3	4	5	6	7	8	9
Name	B. J.	G. J.	C. E.	M. J.	E. M.	G. H.	M. W	K. W	U. O.
Declaration, present	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg	Neg.	Pos.
Declaration, past	Neg.	Neg.	Neg.	Pos.	Neg.	Neg.	Neg.	Neg.	Pos.
History	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.
Stomach empty	4½ hrs.	4½ hrs.	5 hrs.	5 hrs.	4½ hrs.	6 hrs.	6 hrs.	6 hrs.	6 hrs.
Greater curvature	Crest	Crest minus 1 inch	Crest plus 1 inch	Crest minus 1 inches	Crest minus 2 inches	Crest minus 5 inches	Crest minus 2 inches	Crest plus 1½ inches	Crest
Transverse colon	Low	Kink	Kink	Low	Low	.....	Kink Low	.....	.....
Intestinal tract empty	72 hrs.	96 hrs.	96 hrs.	96 hrs.	72 hrs.	72 hrs.	72 hrs.	48 hrs.	24 hrs.
Lumen of colon	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Spastic	Normal
Type	Atonic	Atonic	Atonic	Atonic	Atonic	Atonic	Atonic	Spastic	Periodic
Diagnosis	Chronic intestinal atony								

Chronic intestinal stasis, atonic type	7	14
Chronic intestinal stasis, spastic type	1	2
Chronic intestinal stasis, periodic	1	2
Intestinal stasis, total	9	18

50 cases studied

Three patients—6 per cent.—had with the atony of the bowel an associated atony of the stomach.

TABLE 21.—Intestinal Stasis Associated with Gastric Atony

Number	1	2	3
Name	T. P.	T. H.	R. L.
Declaration, present	Negative	Negative	Negative
Declaration, past	Positive	Negative	Negative
History	Positive	Positive	Positive
Stomach empty	6 (plus) hrs.	6 (plus) hrs.	6 (plus) hrs.
Greater curvature	Crest minus 2 in.	Crest minus 2 in.	Crest
Transverse colon	Low	Kinked	
Intestinal tract empty	72 hrs.	120 hrs.	72 hrs.
Lumen of colon	Normal	Normal	Normal
Diagnosis	Chronic gastric and intestinal atony		

Chronic gastric and intestinal atony	3	6 per cent.

50 cases studied

Nine patients—18 per cent.—had with intestinal stasis, chronic inflammatory changes of the mucosa.

TABLE 22.—Intestinal Stasis Associated with Chronic Inflammation

Number	1	2	3	4	5	6	7	8	9
Name	M. P.	H. O.	L. R.	S. J.	K. H.	J. A.	C. L.	D. G.	B. H.
Declaration, present	Neg.	Neg.	Neg.	Pos.	Pos.	Pos.	Pos.	Neg.	Neg.
Declaration, past	Neg.	Neg.	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.
History	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.
Stomach contents, layers	....	....	....	2	2	....	....	3	3
Mucus span	....	....	....	2 inch	2 inch	....	....	2 inch	2 inch
Free HCl	....	....	....	56	55	....	....	50	57
Stool mucus	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Pos.	Pos.	Neg.
Number of stools	2—6	2—5	0—5	0—6	0—6	0—1	1	1—6	2—3
Intestinal tract empty	48 hrs.	72 hrs.	48 hrs.	96 hrs.	72 hrs.	48 hrs.	48 hrs.	48 hrs.	96 hrs.
Diagnosis	Chronic colitis with stasis				Chronic enterocolitis with stasis			Chronic gastro-enterocolitis with stasis	

Chronic colitis with stasis	4	8 per cent.
Chronic enterocolitis with stasis	3	6 per cent.
Chronic gastro-enterocolitis with stasis	2	4 per cent.
Stasis associated with chronic inflammation—total	9	18 per cent.

50 cases studied

Four patients—8 per cent.—had evidences of either secondary or primary irritations, other than as classified in the foregoing.

TABLE 23.—Secondary Gastro-Intestinal Irritation

Number	1	2	3	4
Name	B. W.	G. J.	C. O.	H. L.
Declaration, present	Positive	Negative	Positive	Negative
Declaration, past	Positive	Negative	Positive	Negative
History	Positive	Suggestive	Positive	Positive
Titration free HCl	59	67	71	
Stomach content after 50 minutes	100 c.c.	65 c.c.	60 c.c.	
Quotient	90 / 20	21 / 44	45 / 15	
Empty stomach	10 c.c.	25 c.c.	35 c.c.	
Mucus in stomach	Negative	Positive	Positive	
Occult blood in stomach	Negative	Negative	Negative	
Occult blood in stool	Negative	Negative 1 Positive 1	Negative 1 Positive 1	3 or 4 stools daily every week or two
Diagnosis and Remarks	(Two attacks jaundice with pain). History and physical examination makes gallstones most likely	Interstitial hepatitis, alcoholic; large liver 2 cm. below costal arch; firm; food remained in cecum; transverse and descending colon empty	Pylorus sharply flexed on lesser curve; cap not distinct; 6 hrs. no retention; peptic ulcer suggested	Meat in diet causes cramps and 3 or 4 stools a day; frequent attacks, suggestive of a pancreatic disturbance

Possible gallstones	1	2 per cent.
Possible interstitial hepatitis, alcoholic	1	2 per cent.
Possible pyloric ulcer	1	2 per cent.
Possible pancreatic insufficiency	1	2 per cent.
Secondary gastro-intestinal irritation—total	4	8 per cent.

50 cases studied

Many of these twenty-five positive gastro-intestinal irritation cases, were of such high grade severity that it is remarkable that they did not come to our service on admission to the hospital. It is a common experience for patients with gastro-intestinal troubles to complain of palpitation, fast pulse, precordial pain, vasomotor disturbances, spots before the eyes, dyspnea on relatively slight exertion, dizziness or giddiness and complaints of general or local nervousness. Certainly no one would expect the receiving ward to make a careful differentiation of cases showing the N. C. A. syndrome with pronounced symptoms of stomach and bowel troubles from stomach and bowel troubles with resulting or associated nervous manifestations. It is quite possible that these nervous patients, undergoing a new experience in entering the hospital, were having an accelerated pulse, and when the receiving officer asked them their complaints their attention was directed to their hearts, and they were assigned accordingly. On studying this very interesting series I was impressed not only with the fact that 50 per cent. had gastro-intestinal irritations, but also with the large proportion showing other foci of irritation, such as diseased tonsils, numerous

carious teeth, many missing grinders, etc. To all this internal scratching there was added the external irritation of having to leave home and go to camp, there to perform duties for which they had little or no liking. What little nerve capital they had left after these more or less prolonged internal irritations was wiped out by the external irritation, by worry. Their nerves were now without strength. They were neurasthenic. They could have carried the external irritation like other men if it had not been for the internal load.

Removal of all possible foci of irritation surgically and dietetically places them in a condition favorable to reconstruction by graduated exercises. To hasten reconstruction I think it is of considerable importance that these patients be taught practical points about nerve hygiene. They should know how to discipline themselves, something they have never known or practiced; what self-discipline means, its importance, and just how it should be daily practiced; how to conserve their nerve capital which is gradually being acquired, and how to economize the pennies and nickles of nerve force. They will thereby know more of practical value about themselves and become most interested in their own development.

Size of the Heart.—Following the plan of Meakins and Gunson, fifty patients were examined with the view of determining the size of the heart, and comparing with normal controls after Dietlen. As in their report, weight was taken into consideration. Comparison shows the average transverse diameter to be somewhat less in patients than in the controls. What effect a rapid rate has on the heart size of these patients is not definite, since the men studied have not undergone such severe training. We can at least be sure that the cases under consideration show no lesion of an organic nature.

TABLE 24.—Comparing Cardiac Measurements in Patients and Controls

Number	Per Cent.	Weight, Pounds	Average Transverse Diameter by Percussion, in Patients, Cm.	Average Transverse Diameter by Roentgen-Ray, in Patients (72 Inches), Cm.	Average Transverse Diameter in Controls,* Cm.
5	10	110-120	12.1	11.8	11.9
4	8	121-130	12.4	12.6	12.9
10	20	131-140	12.5	12.0	12.9
9	18	141-150	13.5	12.5	12.9
6	12	151-160	14.4	13.1	13.4
11	22	161-170	13.6	12.9	14.3
4	8	171-180	13.4	12.8	14.3
1	2	181-190	14.5	13.5	14.4
Total 50	100	.....	Average 13.3	Average 12.6	Average 13.4

* After Dietlen.

Cardiac Configuration in Health and Disease.—In comparing clinical and roentgen cardiac findings, a definite scale of measurement and configuration was desired. The large amount of clinical material at hand made possible the selection of cases with complicated and uncomplicated valvular lesions. Ten patients of each clinical type were collected and an average taken of the roentgen-ray findings. The configuration used in reading these plates ascribed the first right curve to the vena cava, the second right curve to the right auricle, the first left

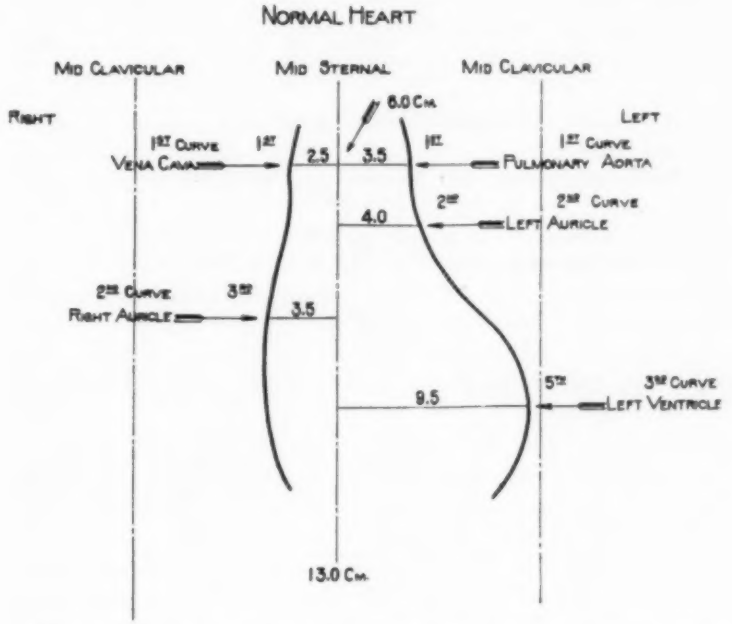

Chart 2.—Plate distance, 72 inches. Scale in this and following charts, 0.5 cm. = 1 cm.

to the pulmonary aorta, the second left to the left auricle and the third left to the left ventricle. In the accompanying configurations (Chart 2) the accentuated second left curve in pure mitral stenosis, the accentuated second and third left curves in combined mitral disease and the increased width of the base of the heart in aortic disease are typical. While measurements to be accurate should depend on the weight of the patient, the measurements in Chart 2 might be considered a fair average for a man of 150 pounds.

TABLE 25.—Comparing Measurements in Health and Disease, from Roentgen Configuration

	Base, Cm.	2nd Left, Cm.	2nd Right, Cm.	3rd Left, Cm.	Transverse, Cm.
Normal heart; average 10 controls.....	6.0	4.0	3.5	9.5	13.0
Mitral insufficiency; average 10 patients..	6.0	4.0	4.0	10.5	14.5
Mitral stenosis; average 10 patients.....	6.0	5.5	4.0	10.0	14.0
Combined mitral insufficiency and stenosis; average 10 patients.....	6.0	8.5	4.5	11.0	15.5
Aortitis chronic with aortic dilatation; average 10 patients	8.0	8.0	5.5	10.0	15.5
Combined aortic and mitral disease; average 10 patients	9.0	8.0	7.0	13.0	20.0

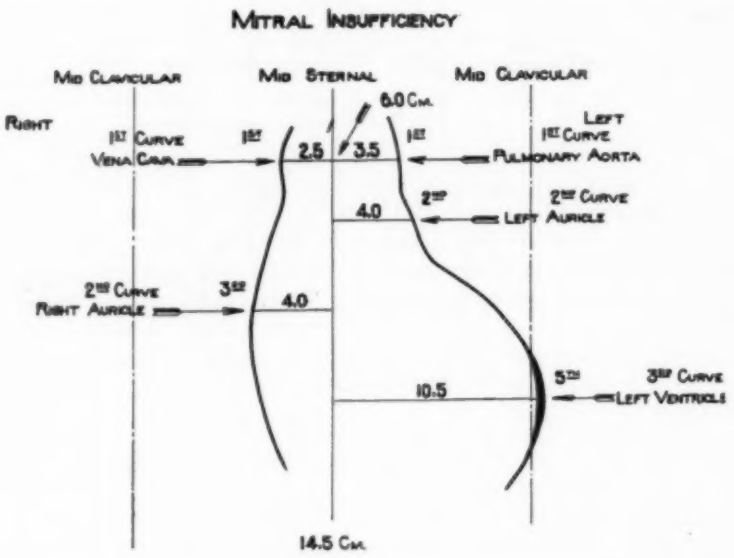

Chart 3.

Comparison of Pulse Rate and Blood Pressure of Patients and Control.—The cardiac rate in patients is somewhat variable, but on taking the average of one group and comparing it with that of others a definite conclusion can be reached. Patients in Group 1, or the first period of training, show a high variable pulse rate with a delayed return to normal. As the higher grade exercises are reached and tolerated, both the rate and response to exercise become more constant and approach more nearly that of the controls.

TABLE 26.—Rest Rate Compared Before and after One Hundred Hops on Left Foot

	Pulse		Blood Pressure		Return to Normal
	Before	After	Before	After	Minutes
Average 10 controls	76	120	124 82	136 84	1½
10 patients, Group 1	96	144	132 84	160 88	3½
10 patients, Group 3	90	132	132 84	160 86	3
10 patients, Group 5	84	128	132 84	156 84	2

Blood pressure readings are also inconstant and show no definite distinguishing feature. The systolic pressure is always somewhat higher in patients than in controls, while the diastolic shows very little difference.

Observations were made on ten men in the final group of training before and after taking a six-mile hike with light pack. This constituted a 90-minute march at a cadence of 120 steps a minute. The response to this test was not unlike that of the controls, three normal men. There was no dyspnea or evidence of distress. These men after a two months course of graduated exercises qualified for full military duty.

TABLE 27.—Rest Rate Before and After Six-Mile Hike with Light Pack

	Pulse		Respiration		Blood Pressure, Systolic		Blood Pressure, Diastolic		Return to Normal, Minutes
	Before	After	Before	After	Before	After	Before	After	
Average 5 controls	76	120	14	16	124	136	82	84	2½
Average 10 patients, Group 5	84	128	16	17	128	144	84	86	2

Effect of Tobacco and Alcohol.—Of the fifty men under observation, 10 per cent. used cigarets to excess (twenty and more daily), 20 per cent. fifteen per day, 30 per cent. moderately (average of ten cigarets per day), 28 per cent. five per day, while 12 per cent. did not use tobacco in any form. In this same group only 4 per cent. admitted alcohol to excess, while 50 per cent. used it moderately, 20 per cent. in slight degree and 26 per cent. had never used it in any form.

Pulse, respiration and blood pressure readings were made before and after smoking five cigarets in succession, the brand used being the

popular Camel. The reaction of ten controls was compared with that of ten men in Group 1, the first period of training, with ten men in Group 3, the midperiod of the course of exercises, and these with ten men of the graduating or final group. Observations on the reaction to exercise were made at the same time, in relation to the effect of smoking. In both patients and controls the pulse and respiratory rate rises after smoking. This, however, was more marked in patients than controls, but men having progressed to the highest grade of exercises reacted only slightly higher than the control, while those in the first class and in the midperiod of training showed a definite reaction. In all observations the reactions were temporary. Only three of the mid-group showed definite aggravation of symptoms, while the controls and the men boarded fit for full duty showed practically no untoward signs.

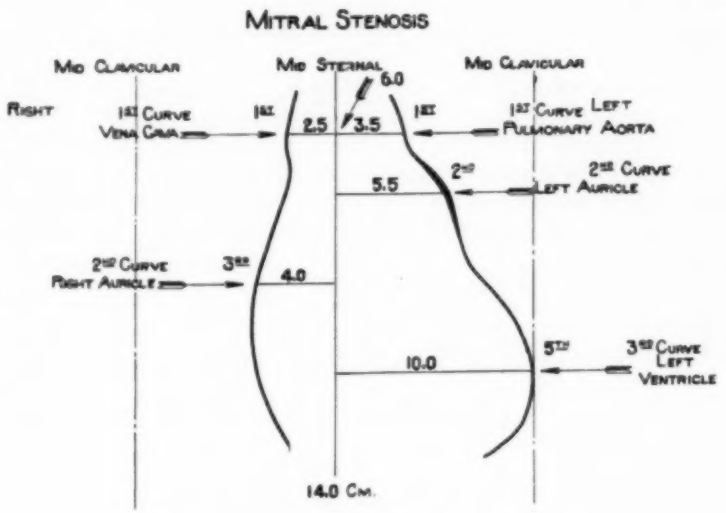

Chart 4.

The 12 per cent. of nonsmokers did not use alcohol. Their symptoms, however, when compared to those of the heavy smokers or excessive drinkers, were not in any way proportionally decreased. Thus, no conclusion can be drawn for a definite basis for production of symptoms. It is therefore evident from our observation that while alcohol and tobacco in excess aggravate the symptoms and signs of this syndrome, they are not a constant primary source of irritation.

TABLE 28.—Observations on Series of Fifty Cases Under Study

Average Consumption of Tobacco		Average Consumption of Alcohol	
Cigarets per Day	Per Cent.		Per Cent.
20	10	Heavy	4
15	20	Moderate	50
10	30	Slight	20
5	28	Total abstainers	26
Nonsmokers	12		

Effect of Cigaret Smoking. — The pulse, respiratory and blood pressure readings were made on ten healthy men before and after smoking five cigarets in succession, and before and after exercise (100 hops on left foot). An average taken of these ten controls shows a normal response to exercise and a very slight reaction as an effect of smoking.

TABLE 29.—Average Effect of Smoking Before and after Exercise in Ten Control Cases

	Pulse		Respiration		Blood Pressure, Systolic		Blood Pressure, Diastolic		Return to Normal, Minutes	
	Before	After	Before	After	Before	After	Before	After	Before	After
Before exercise	72	74	16	18	128	128	84	82	¼	¼
After exercise	108	110	20	22	160	160	88	86	1½	1½

Observations were also made on ten men reporting for the first class of graduated exercises. This constitutes Group 1 in the schedule used. The degree of reaction is greatest in this group when compared with that of the controls. The increased rate is not a marked feature, but three of this group complained of definite breathlessness and a general sense of uneasiness.

TABLE 30.—Average Pulse, Respiration and Blood Pressure in Ten Cases —Group 1—After Graduated Exercises

	Pulse		Respiration		Blood Pressure, Systolic		Blood Pressure, Diastolic		Return to Normal, Minutes	
	Before	After	Before	After	Before	After	Before	After	Before	After
Before exercise	104	108	22	24	144	148	90	90	½	½
After exercise	152	160	24	26	164	180	92	96	3½	4

In Table 30 we find the resting rate high, with an exaggerated response to exercise. There are many stimuli which influence the resting rate. Smoking does this temporarily and to a mild degree. The same effect is produced by a slight change of posture or emotion, so that it is rather difficult to arrive at a fixed average rate for this group.

The average pulse, respiratory and blood pressure readings of ten patients in Group 3, the midperiod of training, are less variable and the reaction to smoking when compared with that of the controls is less marked.

TABLE 31.—Average Pulse, Respiratory and Blood Pressure Readings in Ten Cases—Group 3

	Pulse		Respiration		Blood Pressure, Systolic		Blood Pressure, Diastolic		Return to Normal, Minutes	
	Before	After	Before	After	Before	After	Before	After	Before	After
Before exercise	96	104	20	22	142	146	88	90	½	½
After exercise	134	132	24	26	156	160	92	92	3	3½

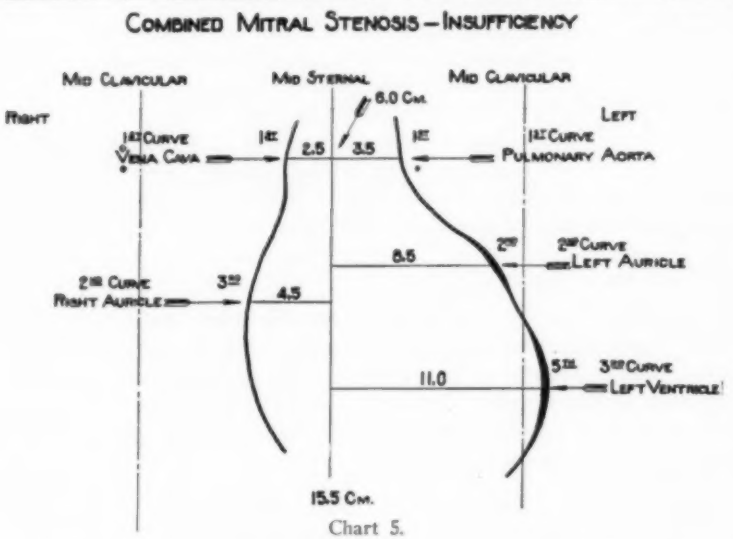

Chart 5.

Group 5, consisting of men having progressed to the highest grade of exercises and who have tolerated them in conjunction with route marches without distress, compare most favorably with the ten controls. Here again the reaction to smoking is slight and the response to exercise only moderately exaggerated by external stimuli.

TABLE 32.—Averages in Ten Cases—Group 5

	Pulse		Respiration		Blood Pressure, Systolic		Blood Pressure, Diastolic		Return to Normal, Minutes	
	Before	After	Before	After	Before	After	Before	After	Before	After
Before exercise	84	88	18	19	136	140	84	88	¼	¼
After exercise	118	122	22	24	144	148	86	88	2	2½

In summarizing, the tobacco reaction, pulse and respiratory and blood pressure readings were slightly higher in patients than controls. Patients in Group 5 compared most favorably with the controls, while those in Group 1 reacted in greater degree. Group 3, in accordance with their tolerance to exercise, reacted in moderate degree.

Effect of Atropin on the Heart Rate.—Observations were made on ten patients compared with ten controls before and after the administration of 1/30 grain atropin sulphate subcutaneously. The response to exercise (one hundred hops on the left foot) before and after atropinization was also noted. Twenty-five minutes were allowed to intervene for complete effect. Both patient and control showed the same results, namely, increased pulse rate approximately to the same degree following atropin. From this Lewis[2] concludes that the high cardiac rate in patients is not due to a reduction in vagal tone, but is more probably due to hyperirritability of some portion of the system including the accelerator reflex arc.

The patients presented for observation before administration of atropin showed marked dermatographia, cold, clammy, cyanotic hands and marked axillary sweating. After atropinization this picture was entirely changed, much to the surprise of the patients. Hands were dry, pink, hot and the dermatographia temporarily disappeared.

TABLE 33.—Effect of Atropin on Ten Patients

Atropin, 1/30 Gr.	Rest Rate		After Exercise		Blood Pressure at Rest		Blood Pressure After Exercise	
	Before	After	Before	After	Before	After	Before	After
Average 10 controls.....	80	108	132	144	128 80	132 84	140 80	152 86
Average 10 patients.....	88	118	128	158	132 84	136 84	146 86	160 88

Thus, in our search for irritation it was determined that the mechanism by which increased rate of patients is arrived at is not altered vagal tone, but a hyperirritability of the system, including the accelerator reflex arc.

TABLE 34.—Foci of Irritation

	No.	Per Cent.		No.	Per Cent.
General physical.....	14	28	Psychiatric.....	6	12
Thyroid.....	10	20	Neurologic.....	34	78
Ear.....	4	8	Gastro-intestinal.....	25	50
Nose.....	16	32	Genito-urinary.....	6	32
Sinuses.....	10	20	Syphilis.....	2	4
Throat.....	45	90	Alcohol.....	4	8
Teeth.....	18	36	Tobacco.....	5	10

2. Report by Cotton, Rapport, Lewis.

Weights.—During the entire period of training, weights were taken at six-day intervals. All men gained weight rapidly up through the group, including the highest grade of exercises. When route marches were taken in conjunction with the high grade exercises, without and with light and full pack, an average of one-half pound per man was lost from the admission weight.

TABLE 35.—Weight Gained During Period of Training

Pounds	No.
Constant	5
1	1
2	1
3	1
4	2
5	2
7	2
Total	14

28 per cent. gained weight

TABLE 36.—Weight Lost During Period of Training

Pounds	No.
1	5
2	10
3	4
4	5
5	1
6	4
7	4
9	2
10	1
Total	36

72 per cent. lost weight

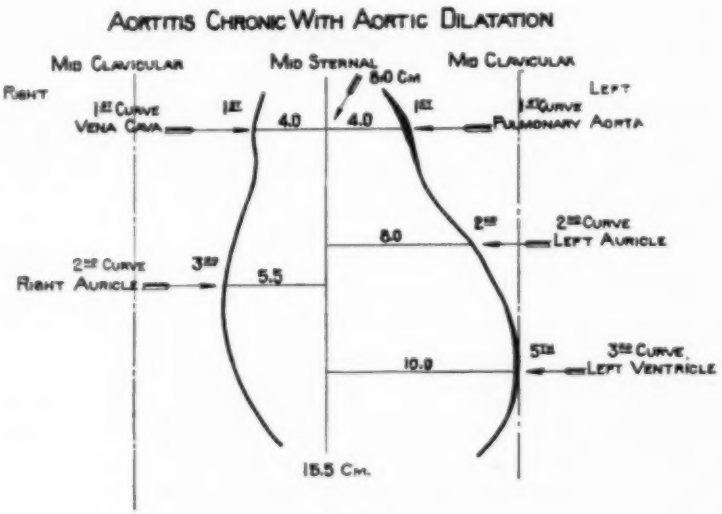

Chart 6.

Final Disposition of Group Progress.—In accordance with our policy of graduated exercises, the fifteen men who progressed to the highest grade exercises and carried them out without distress in conjunction with route marches of 6 miles, with full pack, were sent to

full and unrestricted military duty. These men had no complaints to offer and while there still remained some vasomotor instability, they were decidedly less sensitive to external stimuli, most of the internal foci having been removed, and they had learned that discipline and economy were necessary factors in the march to increased nerve capital. The twenty-five men who progressed more slowly, but toler-

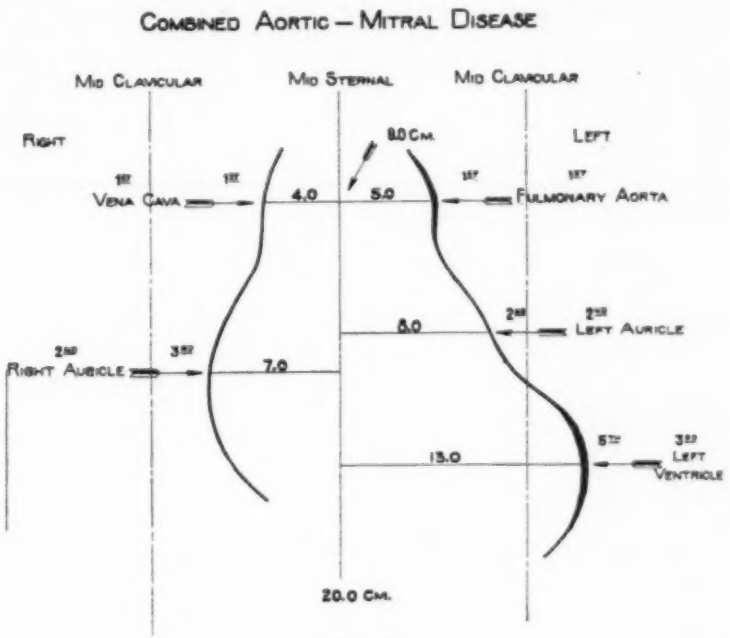

Chart 7.

ated the exercises and route marches without undue distress, were sent to unrestricted domestic duty. An attempt was made to place these men in service according to their individual qualifications, in order that external stimuli be in some meaure eliminated and that conservation and economy of nerve force be promulgated. The ten men showing continued symptoms on the highest grade exercises, but who progressed through all the stages, including route marches, were sent to limited domestic service. Of the group of fifty under study it was not considered necessary to discharge any man as permanently unfit.

TABLE 37.—NEURO-CIRCULATORY ASTHENIA: DATA OF INTENSIVE STUDY OF FIFTY CASES

No.*	Age, Years	Service, Years	Foci of Irritation																		Weight on Admission, Lbs.	Weight on Discharge, Lbs.	Occupation	Observation Time, Days	Group Progress and Disposition
			Thyroid	General Physical	Cardiac	Gastro-Intestinal	Psychiatric	Neurologic	Ear, Nose, Throat	Dental	Roentgen-Ray	Blood	Urine	Stool	Stomach Contents	Genito-Urinary	Wassermann	Prostatic Smear	Tobacco	Alcohol					
1	26	8/12	+	+	−	−	−	+	+	−	−	−	−	−	−	−	−	−	+	−	165	162	Clerk	62	Lim. domestic
2	26	8/12	−	+	−	+	−	+	+	−	−	−	−	−	−	−	−	−	−	−	159	155	Farmer	62	Lim. domestic
3	32	7/12	−	+	−	+	−	−	+	−	−	−	−	−	−	+	−	−	−	−	129	129	Bookkeeper	62	Lim. domestic
4	22	8/12	−	−	−	−	−	+	+	+	−	−	−	−	−	−	−	−	−	−	161	160	Farmer	62	Full duty
5	23	7/12	−	+	−	+	+	+	+	+	+	−	−	+	+	−	−	−	−	−	140	133	Farmer	62	Lim. domestic
6	25	7/12	−	−	−	+	+	+	+	−	+	−	−	+	+	−	−	−	−	−	166	164	Farmer	62	Lim. domestic
7	23	3/12	−	+	−	+	−	+	+	+	+	+	−	−	−	−	+	−	−	−	156	163	Engineer	62	Full domestic
8	22	3/12	−	−	−	−	−	+	+	−	−	−	−	−	−	−	−	−	−	−	149	154	Farmer	62	Full duty
9	30	7/12	−	+	−	+	−	+	+	−	−	−	−	−	−	+	−	−	−	−	158	149	Plumber	56	Full domestic
10	29	1/12	−	−	−	−	−	+	+	+	−	−	−	−	−	−	−	−	−	−	152	155	Constable	56	Full domestic
11	31	7/12	−	−	−	−	−	+	+	−	−	+	−	−	−	+	−	−	−	−	151	149	Printer	56	Full domestic
12	22	7/12	−	+	−	+	−	+	−	+	+	+	−	+	+	−	−	−	−	−	145	141	Farmer	56	Full duty
13	30	1/12	−	+	−	+	+	+	+	−	−	−	−	−	+	−	−	−	+	−	172	171	Laborer	56	Lim. domestic
14	24	7/12	+	−	−	+	−	+	+	−	+	+	−	−	−	+	+	−	+	−	145	144	Clerk	56	Full domestic
15	30	2/12	−	−	−	+	−	+	+	−	+	−	−	−	−	+	−	−	−	−	168	175	Clerk	54	Full duty
16	28	1/12	+	−	−	+	−	+	+	−	−	+	−	−	+	+	−	−	−	−	180	174	Attorney	54	Full domestic
17	25	4/12	−	−	−	+	−	−	+	+	+	+	−	−	−	−	−	−	−	−	142	142	Optician	62	Full domestic
18	27	9/12	+	+	−	−	−	+	−	+	−	+	−	−	−	−	−	−	−	−	136	135	Mechanic	62	Full domestic
19	23	8/12	−	−	−	+	−	−	+	−	−	−	−	+	−	−	−	−	−	−	169	165	Clerk	62	Full duty
20	22	9/12	+	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	115	109	Farmer	62	Full domestic
21	24	2/12	+	−	−	−	+	−	+	−	−	−	−	−	−	−	−	−	−	−	179	170	Farmer	62	Full domestic
22	26	1/12	−	−	−	+	−	+	+	−	+	+	−	−	−	−	−	−	−	−	122	120	Mechanic	62	Full domestic
23	23	2/12	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	159	160	Architect	34	Lim. domestic

24	20	8/12	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	155	148	Jeweler	62	Full duty
25	25	6/12	—	+	—	—	—	—	+	+	—	+	—	—	—	+	—	—	—	—	—	132	126	Clerk	62	Full duty
26	24	5/12	+	+	—	+	—	—	+	+	+	—	—	—	—	—	—	—	—	—	—	138	134	Typist	62	Full domestic
27	24	8/12	—	—	—	+	—	+	+	—	—	—	—	—	—	—	—	—	—	+	+	148	146	Laborer	62	Full duty
28	22	7/12	+	—	—	+	—	+	+	—	+	—	—	—	+	—	—	—	—	—	—	141	137	Lineman	62	Full duty
29	26	2/12	—	—	—	+	—	—	+	+	—	—	—	—	+	—	—	—	—	—	+	175	165	Typist	62	Full duty
30	29	7/12	—	+	—	—	—	+	—	—	—	—	—	—	—	—	—	—	—	—	—	134	127	Builder	62	Full domestic
31	22	14/365	—	—	—	+	—	—	+	—	—	+	—	+	—	—	—	—	—	—	—	133	140	Barber	62	Full duty
32	30	8/12	—	—	—	+	—	+	—	—	+	+	—	+	+	—	—	—	+	+	—	129	122	Clerk	62	Full domestic
33	29	8/12	+	—	—	—	—	—	—	+	—	—	—	—	—	+	—	—	—	—	—	159	164	Laborer	53	Full duty
34	24	1/12	—	—	—	—	—	+	+	—	—	—	—	—	—	+	—	—	—	—	—	137	137	Engineer	53	Full duty
35	26	1/12	—	—	—	+	—	+	+	+	—	—	—	—	—	+	—	—	—	—	—	116	120	Farmer	52	Full domestic
36	23	8/12	—	—	—	+	—	+	+	—	—	—	—	+	—	+	—	—	—	—	—	155	150	Carpenter	52	Full domestic
37	34	8/12	—	—	—	—	—	—	+	—	—	+	—	—	—	—	—	—	—	—	—	142	139	Artist	52	Lim. domestic
38	23	1/12	—	—	—	+	—	+	+	—	—	+	—	+	+	—	—	—	—	—	—	116	114	Miner	52	Full domestic
39	23	2/12	—	—	—	—	—	+	+	+	—	—	—	—	—	—	—	—	—	—	—	137	135	Clerk	52	Full domestic
40	26	8/12	—	—	—	—	—	—	+	—	+	—	—	—	—	+	—	—	—	—	—	143	141	Carpenter	52	Full domestic
41	25	2/12	—	—	—	+	—	+	+	+	—	—	—	+	—	—	—	—	—	—	—	159	157	Miner	52	Full domestic
42	22	1/12	+	—	—	+	—	+	+	—	—	—	—	+	—	—	—	—	—	—	—	137	137	Lineman	52	Full domestic
43	23	1/12	—	—	—	—	—	+	+	+	—	—	—	—	—	+	—	—	—	—	—	121	121	Mechanic	52	Full duty
44	27	1/12	—	—	—	+	—	+	+	+	—	—	—	+	+	+	—	—	—	—	—	170	168	Carpenter	52	Full domestic
45	24	2/12	—	—	—	+	—	+	+	—	—	—	—	—	—	+	—	—	—	—	—	137	134	Farmer	52	Full duty
46	28	2/12	—	—	—	—	+	—	+	+	—	+	—	—	—	—	—	—	—	—	+	168	165	Bartender	48	Full domestic
47	24	8/12	—	+	—	—	+	—	+	—	—	—	—	—	—	—	—	—	—	—	—	146	144	Farmer	47	Full domestic
48	25	1/12	—	+	—	—	—	+	+	+	—	—	—	—	—	+	—	—	—	—	—	118	112	Clerk	42	Lim. domestic
49	25	1/12	—	—	—	—	—	+	+	—	—	+	—	—	—	—	—	—	—	—	—	127	129	Farmer	42	Lim. domestic
50	22	8/12	—	—	—	+	—	+	+	—	—	+	—	—	—	—	—	—	—	—	—	165	169	Clerk	42	Full domestic

* All privates except 14 (sergeant) and 19 and 43 (corporals).

TABLE 38.—Disposition of Men in Groups Studied

	No.	Per Cent.
Unrestricted military duty	15	30
Group progress, good.		
Unrestricted domestic duty	25	50
Group progress, good; highest grade exercises tolerated less perfectly.		
Ordnance	1	
Electrician	1	
Shoe repair	1	
Drill instructors	3	
Typists	4	
Teamsters	4	
Carpenters	3	
Motor truck repair	3	
Pipe fitter and plumbers	1	
Cook	1	
Printer	1	
Laborers	2	
Limited domestic service	10	20
Group progress, fair; highest grade exercises only fairly well tolerated.		
Artist illustrators	2	
Clerks	3	
Medical detachment	1	
Orderlies	2	
Teamsters	2	
Total	50	100

In our early experience with this group all were deemed unfit for military duty, and under former conditions had been withdrawn from their organizations and sent to the Depot Brigade, pending discharge from the National Army. We now return fifty salvaged men to duty, fifteen to unrestricted military duty, twenty-five to unrestricted domestic duty, ten to limited domestic duty.

Our object has been not only to study these men presenting this syndrome from an etiologic and therapeutic point of view, but to prevent any questionable case going overseas, there to become a burden, before subjection to a rigid investigation and graduated method of sorting.

Observation Time.—Fifty per cent. of this group had been in service eight months, 25 per cent. three months, 25 per cent. one month. Under the present system of graduated training and discipline, observation time averaged seven weeks from time of admission to discharge to duty, a saving of six months. This is not only a great difference in time and expense to the government, but to the recruit on whose early training so much depends.

THE EXCRETION OF CREATIN, CREATININ, AND URIC ACID IN ACUTE FEBRILE CONDITIONS*

C. W. McCLURE, M.D.
BETHLEHEM, PA.

The excretion of creatin, creatinin and uric acid in the urine during the course of acute infectious fevers has been studied by Cathcart,[1] Van Hoogenhuyze and Verploegh,[2] af Klercher,[3] Kocher,[4] Shaffer,[5] Ewing and Wolf,[6] Shaffer and Coleman,[7] and others. Their results agree as regards the finding of creatinuria, and an increased output of creatinin and of uric acid. The diets used by most investigators were at times in the course of the experiments of insufficient caloric value and not particularly rich in carbohydrates. Shaffer and Coleman have investigated the effects of high caloric diets, rich in carbohydrates, on the protein metabolism of patients with typhoid fever. They found that these diets retarded or prevented the loss of body protein in their cases. For this reason it was considered important to study the excretion of certain of the products of protein metabolism in the different varieties of acute febrile conditions at a time when the affected patients were receiving a "Shaffer-Coleman diet." The products chosen were creatin, creatinin and uric acid because of the accuracy with which their endogenous amounts can be determined.

EXPERIMENTAL PROCEDURE

Patients were given the diet proposed by Shaffer and Coleman, except that no purin- or nuclein-containing foods were fed. The diet contained approximately from 3,000 to 4,000 calories of protein, fat and carbohydrate in each day's feeding. Urine specimens were preserved on ice under toluol. Uric acid, creatin, and creatinin were determined by the methods of Folin.[8] In

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1. Cathcart: Uric Acid Output and Heat Production, Proc. Roy. Soc., London, 1907, **79,** 13.
2. Van Hoogenhuyze, C. J. C., and Verploegh, H.: Weitere Beobachtungen über die Kreatininausscheidungen beim Menschen, Ztschr. f. physiol. Chem., 1908, **57,** 162.
3. af Klercher, Kj., O.: Ueber Ausscheidung von Kreatin und Kreatinin in fieberhaften Krankheiten, Ztschr. f. klin. Med., 1909, **68,** 22.
4. Kocher, R. A.: Ueber die Grösse des Eiweisszerfalls bei Fieber und bei Arbeitsleitstung, Deutsch. Arch. klin. Med., 1914, **115,** 82.
5. Shaffer, P.: The Excretion of Kreatinin and Kreatin in Health and Disease, Am. Jour. Physiol., 1908-1909, **23,** 1.
6. Ewing, J., and Wolf, C. G. L.: The Clinical Significance of the Urinary Nitrogen, THE ARCHIVES INT. MED., 1909, **4,** 330.
7. Shaffer, P. A., and Coleman, W.: Protein Metabolism in Typhoid Fever, THE ARCHIVES INT. MED., 1909, **4,** 538.
8. Folin, O.: On the Determination of Creatinin and Creatin in Urine, Jour. Biol. Chem., 1914, **17,** 469. A Laboratory Manual of Biological Chemistry, New York, 1916, p. 93.

determining uric acid the "uric acid reagent" was used instead of the "uric acid-phenol reagent." Otherwise the method was employed as given in Folin's manual. Phosphorus was quantitated by the uranium acetate titration method. All temperatures recorded in the appended table are rectal temperatures. A total of eight febrile conditions has been studied, comprising six cases of typhoid fever, four cases of lobar pneumonia, one case of streptococcic bronchopneumonia, two cases of tuberculous bronchopneumonia, two cases of pulmonary tuberculosis, one of which was complicated by hemopneumothorax, one case of subacute rheumatic fever, and two cases with fever of unknown cause.

The Relation of Creatinuria to Fever.—Creatinuria was present throughout the febrile periods in two cases (2, 3, see table). In another case (1) the output of creatin ceased nine days prior to the disappearance of the pyrexia. In one case creatinuria was present during one period of fever and absent throughout the course of a second febrile period in this patient (5). Creatinuria was either completely absent or present in small amount in five febrile cases (5, 6, 7, 8, 9). In three of these fever was present over periods of observation of from one to four weeks. Two cases were febrile but a short time. One of these showed no creatinuria, and the other a small amount on two occasions. Another case (12) had very slight creatinuria during two periods of high fever. Postfebrile creatinuria persisted for from seven to ten days in two cases (13, 14), and in three others (2, 5, 12) it was present for a few days.

These findings show that there was no constant relation between the presence of pyrexia and creatinuria.

The Relation of Creatinuria to Loss in Body Weight.—In seven cases loss in body weight was accompanied by creatinuria (1, 2, 3, 4, 10, 13, 14). In three of these (3, 13, 14) creatin did not disappear from the urine with the cessation of the loss in body weight. In one case (3) creatinuria was present during weeks in which there was very little or no loss in weight, as well as during the time when rapid loss occurred. One patient (12) had slight creatinuria during a period of loss in weight and again during a period when there was a gain in weight. Two patients showed only an occasional slight creatinuria during periods of moderately rapid loss in body weight.

These findings show that the presence of creatinuria, although usually occurring coincidently with loss in body weight, is not definitely related to either the rapidity or the amount of weight lost.

The Relation of Creatinuria to the Increase in the Excretion of Creatinin and of Uric Acid.—Creatinuria was associated with disturbances in the excretion of both creatinin and uric acid in four cases (2, 3, 14, 15). In two cases (4, 13) there was a considerable amount of creatin excreted while the output of creatinin remained normal. In all but one case in which creatinuria occurred there was also an increased elimination of uric acid. In this case (12) there was a slight creatinuria, which was not accompanied by an abnormal crea-

tinin or uric acid output. These findings show that during periods of pyrexia creatinuria may occur unaccompanied by disturbances in the excretion of uric acid and of creatinin.

Creatinin.—In most cases the amounts of creatinin excreted were increased during the periods of pyrexia. This increase was often present only at irregular intervals. In one case (9) the disturbance in the output of creatinin was as great during the afebrile as during the febrile period. In two cases (11, 12) no increase in the amounts of creatinin excreted occurred in spite of the presence of high fever. A disturbance in the excretion of creatinin was found in one case (9) without associated anomalies in the elimination of uric acid or of creatin. These findings demonstrate that in certain of the febrile diseases, (*a*) disturbances in the excretion of creatinin are not necessarily associated with an increase of the body temperature, and (*b*) that such disturbances may occur independently of anomalies in the excretion of uric acid and creatin. An increase in the output of creatinin was not related to loss of body weight in all cases.

Uric Acid.—In all but two cases uric acid was excreted in abnormally large amounts during the periods of pyrexia (9, 12). A postcritical increase in the amounts of uric acid eliminated persisted over periods of from five to nine days in five cases (1, 14, 16, 17, 18). Creatinuria was present in three of these cases, in one of which an increased creatinin output, also, occurred. No examination for creatin in the urine was made in the other two cases. In one case (18) an increase in the excretion of phosphorus accompanied the enlarged output of uric acid. These findings show that an increase in the output of uric acid during the course of the acute infectious diseases is not wholly dependent on the presence of pyrexia. In this connection it is interesting to note that Mandel[9] found a decrease in the output of uric acid in three cases of "aseptic fever."

In six cases (1, 2, 9, 12, 14, 17) anomalies in the excretion of one of the three substances studied occurred during the second or the third week of convalescence. No definite relationship was found between the severity of the symptoms manifested by the patients and the amounts of creatin, of creatinin and of uric acid found in the urine.

SUMMARY AND DISCUSSION

Endogenous creatinin and creatin are considered as products of the metabolism of muscular tissue. An increase in the amount of creatinin excreted may be regarded as evidence of an increase of katabolism in the muscles, or possibly of an actual destruction of that tissue. The significance of creatinuria is not definitely known. In

9. Mandel, A. R.: Xanthin as a Cause of Fever and Its Neutralization by Salicylates, Am. Jour. Physiol., 1907-1908, **20,** 439.

view of the work of Folin[10] and of Denis[11] the creatinuria observed in the experiments here reported can readily be explained as the result of an over-production of creatin. "If so much creatin is manufactured that the muscles become supersaturated, creatin is excreted by way of the kidneys."[11] On the other hand, there are some observers[12] who support the view that creatinuria is an expression of an incomplete oxidation of creatin in the body. Acidosis may play a rôle in the production of creatinuria.[13] However, no studies concerning the presence of acidosis were made during the course of the experiments here reported. The origin of endogenous uric acid from the nucleoprotein of the body tissues is fairly well established. It is impossible to ascertain the exact source of the nucleoprotein from which the excess of uric acid, found during the course of these experiments, was derived. The increase in the elimination of uric acid was no greater in those diseases accompanied by leukocytosis than in those in which this did not occur. This finding shows that the disintegration of leukocytes played a minor rôle in its production. Nevertheless, it is fair to assume that a certain amount of the excess of the uric acid eliminated during the stage of resolution in pneumonia was derived from the absorption of the pulmonary inflammatory exudate. However, a postcritical increase in the output of uric acid occurred in other disease conditions in which no such exudate was present. Also, it was not found in two of the cases of lobar pneumonia studied, but in these cases the areas of pulmonary consolidation were small. A postcritical increase in the excretion of uric acid was accompanied, in certain cases, by creatinuria and an excessive output of creatinin. The latter two phenomena would not result from the breaking down of cellular inflammatory

10. Folin, O., and Denis, W.: Protein Metabolism from the Standpoint of Blood and Tissue Analysis. VII. An Interpretation of Creatin and Creatinin in Relation to Animal Metabolism, Jour. Biol. Chem., 1914, **17,** 493.

11. Denis, W.: The Influence of the Protein Intake on the Excretion of Creatin in Man, Jour. Biol. Chem., 1917, **30,** 47. Denis, W., and Kramer, J. G.: The Influence of Protein Intake on Creatin Excretion in Children, Jour. Biol. Chem., 1917, **30,** 189. Denis, W., and Minot, A. S.: The Production of Creatinuria in Normal Adults, Jour. Biol. Chem., 1917, **31,** 561.

12. Mendel, L. B., and Rose, W. C.: Experimental Studies on Creatin and Creatinin. I. The Rôle of the Carbohydrate in Creatin-Creatinin Metabolism, Jour. Biol. Chem., 1911-1912, **10,** 213. Benedict, S. R., and Osterberg, E.: Studies in Creatin and Creatinin Metabolism. III. On the Origin of Urinary Creatin, Jour. Biol. Chem., 1914, **18,** 195. Rose, W. C.: Experimental Studies on Creatin and Creatinin. V. Protein Feeding and Creatin Elimination in Pancreatic Diabetes, Jour. Biol. Chem., 1916, **26,** 331. Rose, Mary S.: Creatinuria in Women, Jour. Biol. Chem., 1917, **32,** 1. Janney, N. W., Goodhart, S. P., and Isaacson, V. I.: The Endocrine Origin of Muscular Dystrophy, THE ARCHIVES INT. MED., 1918, **21,** 188.

13. Underhill, F. P.: Studies in Creatin Metabolism. I. Possible Interrelation Between Acidosis and Creatin Elimination, Jour. Biol. Chem., 1916, **27,** 127. Underhill, F. P., and Baumann, E. J.: Studies in Creatin Metabolism. IV. The Relationship of Creatinuria to Carbohydrate Metabolism and Acidosis, Jour. Biol. Chem., 1916, **27,** 151.

exudates. They would result from a disturbance in muscular metabolism. These evidences of postcritical disturbances in metabolism warrant the conclusion that the excess of uric acid excreted during this period was, in part, derived from the nucleoprotein of the body tissues and not wholly from the absorption of cellular inflammatory exudates.

It was found that creatinuria, or an increased output of creatinin, or of uric acid may each occur singly or in any combination with each other. This indicates that there is not an inseparable relationship between the metabolisms of these three substances.

The inconstant occurrence of creatinuria, and, to a less extent, of an increase in the outputs of creatinin and of uric acid, in the presence of pyrexia may, in part, be explained by the sparing action of carbohydrate on the body protein. The latter is well illustrated in the work of Shaffer and Coleman, and of Graham and Poulton.[14] The former investigators did their work on typhoid fever patients, and the latter on normal men in whom pyrexia was induced by exposure to unusually high temperatures. From their results they concluded that the loss of body protein could be retarded or prevented during periods of pyrexia by the use of high caloric diets rich in carbohydrates. In spite of such diets, and in spite of the absence of weight loss, disturbances in the excretion of creatin, of creatinin and of uric acid were not always absent in the experiments here reported. It therefore seems probable that these disturbances were, in part at least, an expression of the effect of toxins. This view is supported by the studies of Dubois and his co-workers.[15] The findings of these investigators indicate that in typhoid fever and malaria a toxic destruction of protein occurs. Whether toxins act by increasing katabolism or by actual disintegration of body tissue is not definitely known. The disintegration of body tissue would seem to be unusual in patients receiving high caloric diets and who are not losing weight, either during periods of pyrexia or, especially, during convalescence. Nevertheless, it must be borne in mind that certain pathologic structural changes occur in the different body tissues in the presence of continued pyrexia. The relation of these degenerative changes to the presence of creatinuria, and to an increase in the production of creatinin and uric acid are unknown. If such pathologic changes were an important factor in the production of these phenomena, constant relations in the excretion of creatin, of creatinin, and of uric acid would be expected, under comparable experimental conditions. Since the relations in the excretions of these sub-

14. Graham, G., and Poulton, E. P.: The Influence of High Temperature on Protein Metabolism with Reference to Fever, Quart. Jour. Med., 1912, **6,** 82 and 124.

15. Coleman, W., and Dubois, E. F.: Calorimetric Observations on the Metabolism of Typhoid Patients With and Without Food, THE ARCHIVES INT. MED., 1915, **15,** 887. Barr, D. P., and Dubois, E. F.: The Metabolism in Malarial Fever, THE ARCHIVES INT. MED., 1918, **21,** 627.

stances were found to be variable, the degenerative changes occurring in the tissues during pyrexia probably play but a minor rôle in the production of creatinuria, or of an increase in the excretion of uric acid and of creatinin. Therefore, the findings in the experiments here reported support the view that the toxins of the acute infections and of tuberculosis cause an increase in katabolism.

The presence of postcritical creatinuria, of an increased output of creatinin, and of uric acid show that disturbances of metabolism may extend into convalescence. This has been pointed out by Shaffer and Coleman. The occasional recurrence of abnormalities in the excretion of these three substances, after convalescence is well established, suggests that either disturbances in their metabolism are persisting, or that they are easily reproduced.

No creatin was excreted during the course of a very mild case of pneumonia and in certain febrile conditions of short duration which were studied. In severer types of pneumonia, and in long continued febrile states creatinuria was invariably present except in tuberculosis. The apparent rarity of creatinuria in the latter disease may prove, on further study, to be of value in the differential diagnosis of that disease.

The diet used in these experiments was well tolerated. The amounts of creatinin, frequently of creatin, and less often of uric acid, which were excreted were smaller than was to be expected from a comparison of the findings here reported with those of other investigators who did not feed a high caloric diet rich in carbohydrate. Shaffer and Coleman have shown that by the use of such a diet the amount of creatinuria in typhoid patients could be markedly diminished. Loss of weight was slight or completely absent under conditions in which it would naturally be expected. In certain cases an initial loss in weight occurred during the first week in the hospital. It then stopped, although there was no cessation in the symptoms of the disease. These findings show that the "Shaffer-Coleman" diet is a rational adjunct to the treatment of acute febrile diseases.

In selecting patients for study, those without evidences of nephritis were selected as far as this was possible. Certain findings common to nephritis are of frequent occurrence in the presence of fever. The results obtained in those cases in which such findings persisted into convalescence were rejected. The prevention of the loss of a certain number of specimens is very difficult when (1) urine is collected over long periods of time, (2) from acutely ill patients, (3) in the hospital wards. This does not vitiate the results, since the interpretation of findings deals only with abnormally large amounts of the substances studied. For purposes of comparison it is of importance to know the true endogenous level of the substances determined. This can be accomplished by following these determinations well into convalescence, which has been done wherever possible.

CONCLUSIONS

1. Disturbances in the excretion of creatin, creatinin and uric acid during the febrile period of the acute infectious diseases are, largely, an expression of the effect of toxins on metabolism. These disturbances may continue into the period of convalescence.

2. It has been found that the increased excretion of uric acid almost invariably accompanied acute febrile states. It was usually associated either with creatinuria, or with disturbances in the output of creatinin. At times all three phenomena were present.

3. The experimental findings indicate that the loss of uric acid, creatin and creatinin by the body, during acute febrile conditions, is retarded by a high caloric diet rich in carbohydrates.

SYNOPSIS OF CASE REPORTS

CASE 1.—J. J., white, man, aged 34, was admitted to St. Luke's Hospital, Nov. 12, 1917, and discharged recovered, Dec. 19, 1917.

Diagnosis: Typhoid fever.

The past medical history was unimportant. The present illness began three weeks before admission to the hospital, with headache, malaise, lassitude, weakness, epistaxis and diarrhea. These symptoms increased in severity, and two weeks before admission the patient was confined to bed. Nov. 12, 1917, the physical examination was essentially negative. Blood examination, Nov. 12, 1917: hemoglobin, 80 per cent. (Sahli); white cells, 3,440 per c.mm.; differential count, polynuclear leukocytes, 75 per cent., small lymphocytes, 20 per cent., large mononuclears, 5 per cent. The Widal reaction was positive in a dilution of 1:80. Blood culture was sterile. The Wassermann reaction was negative. Weekly examinations of the urine were negative except for the finding of a trace of albumin on one occasion. Phenolsulphonephthalein excretion was 40 per cent. in two hours. Sputum and stool examinations were negative. The course of the disease was uneventful. The patient did not manifest the symptoms of severe toxemia.

CASE 2.—J. M., white, man, aged 35, was admitted to St. Luke's Hospital, Nov. 26, 1917, and discharged recovered, Jan. 8, 1918.

Diagnosis: Typhoid fever.

The previous medical history was unimportant. The present illness began seventeen days prior to entering the hospital, with nausea, vomiting and diarrhea. The patient was not confined to bed until after admission to the hospital. The physical examination on November 26, was essentially negative. Blood examination, November 26: hemoglobin, 90 per cent. (Sahli); white cells, 3,360 per c.mm.; differential count, polynuclear leukocytes 74 per cent., small lymphocytes 16 per cent., large mononuclears 10 per cent. The Widal reaction was positive in a dilution of 1:80. The blood culture showed the typhoid bacillus. The Wassermann reaction was negative. Examinations of the urine showed an occasional trace of albumin during the febrile period but no other pathologic elements. Phenolsulphonephthalein excretion was 60 per cent. in two hours. Examinations of the sputum and feces were negative.

The course of the disease was uneventful. At times a mild delirium was present.

CASE 3.—L. M., white, man, aged 20, was admitted to St. Luke's Hospital, Nov. 29, 1917, and discharged recovered, Jan. 16, 1918.

Diagnosis: Typhoid fever.

The past medical history was unimportant. The present illness began two weeks prior to admission to the hospital, with malaise, lassitude, anorexia, nausea, weakness, and slight epistaxis. November 21 the patient was first confined to bed. November 30 the physical examination was essentially negative. Blood examination, November 29: hemoglobin, 80 per cent. (Sahli); white cells, 5,200 per c.mm.; differential count, polynuclears 70 per cent., small lymphocytes 24 per cent., large mononuclears 5 per cent., eosinophils 1 per cent. The Widal reaction was positive in a dilution of 1:80 and the blood culture showed typhoid bacillli. The Wassermann reaction was negative. Urine examinations were negative, except for a trace of albumin on one occasion. Phenolsulphonephthalein excretion was 60 per cent. in two hours. Examination of the feces was negative.

The only striking feature during the course of the disease was that the hemoglobin fell from 80 per cent. on November 28, to 50 per cent. by December 5, after which date it gradually again increased.

Case 4.—A. F., white, man, aged 47, was admitted to St. Luke's Hospital, Nov. 22, 1917, and discharged recovered, Dec. 24, 1917.

Diagnosis: Rheumatic fever (subacute).

No history was obtainable since the patient spoke only Italian. His physician sent the patient to the hospital with the diagnosis of rheumatic fever. On admission to the hospital the patient complained of pain in the right popliteal space and muscles of the thigh on motion of the leg. Slight pain in the deltoid muscles was caused by motion of the arms There was some stiffness of the fingers and slight pain on motion in the metacarpophalangeal joints. The skin over the knuckle joints was somewhat reddened. The backs of the hands appeared to be swollen but did not pit on pressure. Otherwise, physical examination was negative. Blood examination, Nov. 22, 1917: hemoglobin, 60 per cent. (Sahli); white cells, 25,680 per c.mm. Differential count: polynuclear leukocytes 90 per cent., small lymphocytes 5 per cent., large mononuclears 5 per cent. Blood culture was negative. The Wassermann reaction was positive on two occasions. Urine examinations were negative. Phenolsulphonephthalein excretion was 60 per cent. in two hours.

The meager objective symptoms of arthritis disappeared within a week. Up to within a few days of the subsidence of the fever the patient had occasionally painful joints, but only on motion. The leukocytosis disappeared shortly before the return of the temperature to normal.

Case 5.—J. M., white, man, aged 25, was admitted to St. Luke's Hospital, Nov. 27, 1917, and discharged recovered, Jan. 1, 1918.

Diagnosis: Bronchopneumonia (streptococcic).

The patient spoke only Greek and no history was obtainable. Physical examination, November 28, elicited dulness in the lower right axilla and at the base of the right lung posteriorly. Over these areas breath sounds were almost inaudible and there were numerous fine crackling râles and a pleural friction rub. Over the upper portion of the right chest there were a small number of medium sized crackling râles. Roentgenographic studies showed scattered areas of consolidation throughout the right lung. Blood examination, November 29: hemoglobin, 75 per cent. (Sahli); white cells, 10,000 per c.mm.; differential count, polynuclear leukocytes 74 per cent., small lymphocytes 25 per cent., large mononuclears 1 per cent. December 8, white cells, 9,720 per c.mm., December 19, white cells 24,800 per c.mm. The blood culture on November 28 showed a growth of streptococci, and on December 12, it was negative. During the periods of fever the urine examinations showed a trace of albumin to be present. Phenolsulphonephthalein excretion was 60 per cent. in two hours. Sputum examinations showed no acid fast bacilli. The fever fell by crisis two days after admission of the patient to the hospital. The temperature remained normal for two weeks and then a second febrile period began. The areas of dulness in the chest and the roentgenographic findings

persisted until a short time before the patient was discharged. Throughout the course of the disease symptoms of severe toxemia were not manifested.

CASE 6.—M. M., white, man, aged 19, was admitted to St. Luke's Hospital, Nov. 10, 1917, and discharged improved, Nov. 23, 1917.

Diagnosis: Pulmonary tuberculosis.

The past medical history was unimportant. The present illness had begun nine days prior to admission to the hospital, with headache, backache, anorexia, and a nonproductive cough. Physical examination, November 11, elicited the signs usual of consolidation in the apex of the left axilla. Roentgenograms showed a well defined area of consolidation in the upper lobe of the left lung and smaller areas scattered throughout the remainder of the lung. Blood examination, November 11: hemoglobin, 85 per cent. (Sahli); white cells, 6,960 per c.mm.; differential count, polynuclear leukocytes 70 per cent., small lymphocytes 25 per cent., large mononuclears 5 per cent. The Widal reaction and the blood culture were negative. The Wassermann reaction was positive. Sputum examinations showed no acid fast bacilli. Examinations of the urine and feces were negative. Phenolsulphonephthalein excretion was 60 per cent. in two hours.

The patient had only an occasional slight cough during his stay in the hospital. The fever gradually decreased. There were no complications.

CASE 7.—E. P., white man, aged 27, was admitted to St. Luke's Hospital, Nov. 18, 1917, and discharged improved, Dec. 24, 1917.

Diagnosis: Hemopneumothorax; pulmonary tuberculosis.

The past medical history was unimportant. The history of the present illness was indefinite, since the patient had been on an alcoholic spree prior to admission to the hospital. On physical examination, November 19, there were found signs characteristic of pleurisy with effusion involving the entire left chest. To these signs were added a distinct "coin sound," especially audible over the lower half of the left chest. On thoracentesis air and several hundred cubic centimeters of blood were aspirated from the left pleural cavity. Blood examination, November 19: hemoglobin, 70 per cent.; white cells, 26,720 per c.mm.; differential count, polynuclear leukocytes 72 per cent., small lymphocytes 26 per cent., large mononuclears 2 per cent. The Wassermann reaction was negative. The examinations of the urine were negative except for the occasional finding of a trace of albumin and a hyaline cast. Phenolsulphonephthalein excretion was 60 per cent. in two hours. The sputum examinations showed no acid fast bacilli.

The patient manifested no signs of severe toxemia throughout his stay in the hospital. The physical findings did not change.

CASE 8.—V. I., white man, aged 43, was admitted to St. Luke's Hospital Nov. 29, 1917, and discharged recovered Dec. 19, 1917.

Diagnosis: Fever of unknown cause.

No history obtainable; the patient did not speak English.

Physical examination, November 30, was essentially negative. Blood examination, December 1: hemoglobin, 75 per cent. (Sahli); white cells, 2,520 per cmm.; differential count, polynuclear leukocytes, 60 per cent.; small lymphocytes, 30 per cent.; large mononuclears, 10 per cent. The Widal reaction was negative. Examinations of the feces, sputum and urine were negative.

The course of the patient's disease was uneventful. There were no manifestations of severe toxemia.

CASE 9.—W. C., white, man, aged 27, was admitted to St. Luke's Hospital Dec. 3, 1917, and discharged recovered Jan. 5, 1918.

Diagnosis: Lobar pneumonia (type not determined).

The past medical history was unimportant. The present illness began two days before admission to the hospital, with a chill and pleuritic pain in the left side of the chest. On physical examination, December 14, a small area

of pulmonary consolidation was found in the region of the angle of the scapula in the left back. The roentgenogram showed a small area of consolidation to be present in this region. Blood examination, December 14: hemoglobin, 80 per cent. (Sahli); white cells, 19,000 per cmm.; differential count, polynuclear leukocytes, 78 per cent.; small lymphocytes, 14 per cent.; large mononuclears, 8 per cent. The sputum was mucopurulent and blood tinged. No acid fast bacilli were found. The examinations of the feces and urine were negative. Phenolsulphonephthalein excretion was 60 per cent. in two hours.

The fever fell by lysis. The area of consolidation disappeared after twelve days' stay in the hospital.

Case 10.—A. C., white, man, aged 28, was admitted to St. Luke's Hospital Jan. 9, 1918.

Diagnosis: Tuberculous bronchopneumonia.

The past medical history was unimportant. The present illness began three weeks prior to admission to the hospital, with anorexia, frequent vomiting and much coughing, with a large amount of mucopurulent sputum. On physical examination, January 10, signs of pulmonary consolidation were found at the angle of the scapula, the apex of the axilla and the anterior portion of the right chest. Medium and fine crackling râles were audible throughout both lungs. Blood examination, January 1: hemoglobin, 70 per cent. (Sahli); white cells, 16,480 per cmm.; differential count, polynuclear leukocytes, 70 per cent.; lymphocytes, 26 per cent.; large mononuclears, 4 per cent. Blood culture was negative. The Wassermann reaction was negative. The urine contained a faint trace of albumin, but no other pathologic elements. The sputum contained acid-fast bacilli.

The patient was still under observation January 24. Other than the cessation in the loss in weight his condition remained the same during observation in the hospital.

Case 11.—S. J., white, man, aged 50, was admitted to St. Luke's Hospital Dec. 23, 1917.

Diagnosis: Tuberculous bronchopneumonia.

The past medical history was unimportant. The present illness began two months prior to admission to the hospital with weakness and anorexia. Three days before admission he was seized suddenly with pleuritic chest pain, a productive cough and vomiting. Physical examination, December 24, revealed signs of pulmonary consolidation over the entire front of the right side of the chest. Numerous medium and fine crackling râles were present throughout both lungs. Blood examination, December 24: hemoglobin, 60 per cent. (Sahli); white cells, 10,480 per cmm.; differential count, polynuclear leukocytes, 60 per cent.; lymphocytes, 10 per cent.; large monnouclears, 30 per cent.; red cells, 3,610,000 per cmm. The urine contained a small amount of albumin and a few hyaline casts. The sputum was pneumonic in character and contained acid fast bacilli.

The patient ran a high temperature, varying about 2 degrees from morning to night. January 7 bronchial breathing developed in the right intrascapular region.

Case 12.—J. S., white, boy, aged 12, was admitted to St. Luke's Hospital Dec. 7, 1917, and discharged recovered Jan. 18, 1918.

Diagnosis: Fever of unknown cause.

The past medical history was unimportant. The present illness began one week prior to admission to the hospital, with diffuse abdominal pain, diarrhea and epistaxis. Later, malaise and lassitude developed. On physical examination, December 8, an enlarged, firm, smooth and nontender spleen was palpable at the left costal border. Otherwise physical examination was negative. Roentgenographic studies of the lungs were negative. Blood examination, December

8: hemoglobin, 72 per cent.; white cells, 6,550 per cmm.; differential count, polynuclear leukocytes, 68 per cent.; lymphocytes, 10 per cent.; large mononuclears, 22 per cent.; red cells, 4,160,000 per cmm. The Widal reaction on two occasions was negative, as were also the blood cultures. Examinations of the urine and feces were negative.

The patient had two febrile periods of seven and eighteen days' duration, separated by an interim of a week. He manifested no symptoms of severe toxemia in spite of a high fever. The enlarged spleen disappeared after the second febrile period had ended.

CASE 13.—J. C., white, man, aged 30, was admitted to St. Luke's Hospital Nov. 24, 1917, and discharged recovered Dec. 31, 1917.

Diagnosis: Lobar pneumonia (Type IV).

The past medical history was unimportant. The present illness began one week prior to admission to the hospital, with a chill, pleuritic pain in the chest, cough and bloody, tenacious sputum. Physical examination, November 25, elicited the signs of pulmonary consolidation in the left infraclavicular fossa and the apex of the left axilla. The skin and the sclerae were icteric. Blood examination, November 26: hemoglobin, 60 per cent.; white cells, 36,880 per cmm.; differential count, polynuclear leukocytes, 91 per cent.; lymphocytes, 5 per cent.; large mononuclears, 1 per cent.; eosinophils, 1 per cent.; mast cells, 2 per cent. Blood culture showed pneumococci belonging to Type IV. The Wassermann reaction was negative. Urine examinations showed a small amount of albumin and bilirubin. The sputum was typically pneumonic in type and was deeply bile stained.

The crisis occurred on the fourth day in the hospital. The icterus disappeared on the twelfth day. The signs of pulmonary consolidation had disappeared by December 8, both on physical examination and by the roentgen ray.

CASE 14.—A. B., white, man, aged 23, was admitted to St. Luke's Hospital Nov. 22, 1917, and discharged recovered Dec. 13, 1917.

Diagnosis: Lobar pneumonia (stage of resolution).

No history was obtainable, due to the patient's inability to talk English. The patient entered the hospital during the pneumonic crisis. On physical examination, November 22, there were found the signs of pulmonary consolidation in the entire upper lobe of the right lung. There were numerous medium and fine crackling râles throughout this lung. There was some cough, with mucopurulent, bloody sputum. Blood examination, November 22: hemoglobin, 62 per cent.; white cells, 8 160 per cmm.; differential count, polynuclear leukocytes, 67 per cent.; lymphocytes, 31 per cent.; large mononuclears, 2 per cent. The Wassermann reaction was positive. The urine examinations were negative. Phenolsulphonephthalein excretion was 60 per cent. in two hours. The sputum was mucopurulent and slightly streaked with blood. It did not contain acid fast bacilli.

In about one week the cough and sputum ceased. By December 4 the signs of pulmonary consolidation had disappeared.

CASE 15.—J. G., white, man, aged 35, was admitted to St. Luke's Hospital Dec. 17, 1917, and discharged recovered Jan. 4, 1918.

Diagnosis: Lobar pneumonia.

The patient did not speak English and no history was obtained. On physical examination, December 18, signs of pulmonary consolidation were present in the apex of the right axilla, the right suprascapular fossa and the right intrascapular region. There was no cough and no expectoration. Blood examination, December 7: hemoglobin, 80 per cent.; white cells, 23,000 per cmm.; differential count, polynuclear leukocytes, 93 per cent.; lymphocytes, 2 per

cent.; large mononuclears, 5 per cent. Urine examinations showed occasionally a trace of albumin. Phenolsulphonephthalein excretion was 60 per cent. in two hours.

The crisis occurred the third day in the hospital. The signs of pulmonary consolidation had almost disappeared by December 29, and on January 4 were no longer present.

CASE 16.—P. D., white, boy, aged 20, was admitted to St. Luke's Hospital Nov. 17, 1917, and discharged recovered Jan. 11, 1918.

Diagnosis: Typhoid fever.

The patient did not speak English and no history was obtained. The physical examination was essentially negative. Roentgenographic studies of the lungs were negative. The course of the disease was that of a case of typhoid fever with marked passive delirium. Blood examination, November 17: hemoglobin, 70 per cent.; white cells, 5,040 per cmm.; differential count, polynuclear leukocytes, 68 per cent.; lymphocytes, 19 per cent.; large mononuclears, 13 per cent. Two Widal reactions and two blood cultures were negative. The Wassermann reaction was negative. The urine contained a considerable amount of albumin throughout the period of fever, and also a variable number of casts. These findings disappeared after the fever subsided. Phenolsulphonephthalein excretion was 60 per cent. in two hours. Examination of the feces was negative.

CASE 17.—J. S., white, man, aged 35, was admitted to St. Luke's Hospital Oct. 4, 1917, and discharged recovered Nov. 15, 1917.

Diagnosis: Typhoid fever.

The past medical history was unimportant. The present illness had begun five days prior to admission to the hospital, with malaise, lassitude, anorexia and epistaxis. During this period the patient was confined to bed. On physical examination, October 5, the liver and spleen were palpated at the costal margins. Otherwise the examination was essentially negative. Blood examination, October 5: hemoglobin, 70 per cent.; white cells, 4,000 per cmm. The Widal reaction was positive in a dilution of 1:80. Urine examinations were negative. Phenolsulphonephthalein excretion was 60 per cent. in two hours. The index of urea excretion (McLean) on October 15 was 119 per cent., and on November 1, 243 per cent. Blood urea nitrogen was 8 mg. per 100 c.c. of blood.

The patient had continuous fever for the first five days in the hospital. A recrudescence occurred from the fourteenth to the sixteenth days. The enlarged spleen disappeared with the approach of convalescence. There were no symptoms manifesting severe toxemia.

CASE 18.—G. K., white, man, aged 37, was admitted to St. Luke's Hospital Oct. 2, 1917, and discharged recovered Nov. 10, 1917.

Diagnosis: Typhoid fever.

The past medical history was unimportant. The patient had been confined to bed for the five days prior to admission to the hospital with headache, malaise, chilliness and feverishness. On physical examination, October 3, the spleen was palpated at the left costal margin. Otherwise the examination was essentially negative. Blood examination, October 3: hemoglobin, 80 per cent. (Sahli); white cells, 5,000 per cm.; the Widal reaction was negative. Urine examinations were negative except for an occasional trace of albumin. Phenolsulphonephthalein excretion was 50 per cent. in two hours. The index of urea excretion (McLean) was 276 per cent. on November 1, and the blood urea nitrogen was 7 mg. per 100 c.c.

The patient had fever while under observation for a period of nineteen days. There were no complications and no symptoms of severe toxemia. The enlarged spleen disappeared near the end of the febrile period.

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
1	1	.....	.....	.....	.....	70			
	3	665	0.208	1.107	0.000	..	103.4 101.4	120 100	20 20
	4	1,025	0.308	1.707	0.855	..	102.4 99.6	112 100	24 22
	5	980	0.306	1.399	0.561	..	100.8 98.6	108 96	24 20
	6	570	0.169	0.785	0.194	..	102.0 97.4	100 88	24 14
	7	500	0.156	0.833	0.167	..	100.0 97.8	100 80	24 18
	8	850	0.324	0.944	0.271	62	99.8 97.0	112 92	24 18
	9	950	0.365	1.396	0.323	..	100.4 97.0	92 68	20 18
	10	350+	0.135+	0.438+	0.091+	..	100.0 97.6	104 80	20 18
	11	1,230	0.338	1.538	0.000	..	100.4 97.4	104 84	20 18
	12	905	0.328	1.158	0.000	..	99.8 97.0	108 72	24 18
	13	850	0.333	1.045	0.000	61.5	99.8 97.6	88 60	20 20
	14	965	0.454	1.129	0.000	..	99.0 97.6	92 76	20 20
	15	740	0.418	0.710	0.000	..	99.8 97.0	104 88	20 20
	16	1,065	0.532	1.064	0.000	..	100.0 97.0	102 84	22 20
	17	1,515	0.567	1.030	0.000	..	98.8 98.0	84 80	22 18
	18	1,145	0.508	1.113	0.000	..	98.0 97.0	80 78	20 18
	19	1,750	0.567	1.369	0.000	..	98.4 98.0	88 80	22 20
	20	1,190	0.386	0.992	0.000	..	99.0 97.0	92 80	22 22
	21	1,200	0.361	1.262	0.000	..	99.0 97.0	82 64	20 20
	22	1,515	0.565	1.257	0.000	62	98.0 97.0	84 72	20 20
	23	1,660	0.503	1.160	0.000	..	98.0 97.0	88 76	24 20
	24	1,095	0.469	1.146	0.000	..	100.0 97.0	88 64	20 18
	25	1,840	0.537	1.393	0.000	..	98.8 97.0	88 76	20 18
	26	1,405	0.445	1.033	0.000	..	98.0 97.0	76 64	20 18
	27	2,075	0.481	1.331	0.000	..	98.0 97.4	88 76	22 20

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
1 (cont.)	28	1,535	0.408	1.031	0.000	64	98.0 97.0	84 76	20 20
	29	2,305	0.435	1.122	0.000	..	98.0 97.4	88 76	22 18
	30	1,135	0.313	0.885	0.000	..	99.0 97.8	80 76	24 24
	31	2,105	0.526	2.589	0.000	..	98.0 97.0	88 76	24 20
	32	2,055	0.485	1.399	0.000	..	98.6 97.0	80 74	22 20
	33	1,500	0.378	1.230	0.000	..	99.0 97.0	80 80	22 22
	34	1,820	0.484	1.281	0.000	..	98.6 97.0	88 80	20 20
	35	1,520	0.362	1.085	0.000	..	98.6 97.0	80 80	20 20
	36	2,350	0.470	1.204	0.000	66	97.0 97.0	84 80	20 20
2	1	.....	.....	.....	.....	59			
	2	710	0.422	0.985	0.436	..	104.0 103.0	102 92	24 20
	3	800	0.444	1.000	0.328	..	105.0 102.0	108 92	24 24
	4	925	0.467	1.165	0.240	..	103.8 102.0	112 72	24 24
	5	1,000	0.495	1.338	0.223	..	104.0 102.0	108 100	24 24
	6	1,530	0.819	1.818	0.249	..	104.0 102.4	112 96	28 24
	7	1,390	0.729	1.654	0.276	..	104.0 102.0	112 100	28 24
	8	1,470	0.771	1.633	0.250	58	104.0 101.8	118 88	26 24
	9	1,465	0.813	1.628	0.203	..	104.4 102.6	116 100	28 24
	10	1,300	0.755	1.625	0.231	..	104.6 102.8	128 100	34 24
	11	1,240	0.670	1.515	0.138	..	104.4 102.8	128 112	32 24
	12	995	0.682	1.154	0.219	..	104.0 101.8	136 112	30 24
	13	1,240	0.715	1.304	0.236	..	104.0 101.4	122 110	26 24
	14	1,340	0.334	1.241	0.334	..	100.4 100.0	124 100	24 24
	15	650	0.338	0.722	0.000	57	103.0 100.8	112 96	24 24

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
2 (cont.)	16	1,335	0.635	1.508	0.020	..	101.8 99.8	120 88	24 22
	17	1,060	0.331	1.000	0.116	..	102.6 99.0	116 80	30 24
	18	1,070	0.310	1.124	0.064	..	100.4 98.0	100 84	24 24
	19	880	0.252	0.830	0.191	..	99.8 98.6	100 88	24 24
	20	1,400	0.448	1.000	0.116	..	99.0 98.6	100 80	24 24
	21	1,100	0.300	0.979	0.121	..	99.0 97.8	88 80	24 24
	22	1,180	0.363	1.000	0.000	54.7	99.0 98.0	84 80	20 20
	23	1,395	0.430	1.074	0.222	..	99.0 98.0	96 80	24 20
	24	2,005	0.539	1.082	0.000	..	99.0 97.8	108 80	24 20
	25	1,490	0.387	1.064	0.000	..	99.0 98.4	100 80	24 20
	26	1,770	0.393	1.011	0.000	..	99.4 98.4	100 80	24 18
	27	1,905	0.401	1.011	0.128	..	99.4 98.4	96 80	24 20
	28	1,615	0.349	1.153	0.000	..	102.0 98.4	94 80	24 20
	29	1,635	0.383	1.079	0.000	56.5	100.0 97.6	92 72	24 20
	30	1,605	0.376	1.064	0.000	..	99.4 98.4	92 84	24 20
	36	.....	.....	.....	.....	57			
3	1	.....	.....	.....	.....	54.5			
	3	1,010	0.532	1.772	0.303	..	104.6 102.4	112 100	24 24
	4	2,005	0.783	2.228	0.000	..	105.0 103.0	120 108	24 24
	5	2,530	0.573	1.362	0.098	..	104.8 102.0	120 110	28 24
	6	2,995	0.705	3.411	0.295	..	104.6 102.8	120 108	28 24
	7	1,900	0.760	1.727	0.393	..	104.6 102.4	128 104	26 24
	8	2,645	0.777	1.762	0.360	..	104.4 102.8	124 108	28 24
	9	1,030	0.362	0.903	0.241	48	104.8 102.8	132 108	28 24
	10	1,515	0.765	1.515	0.321	..	104.4 103.0	132 104	28 24

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
3 (cont.)	11	1,130	0.582	1.478	0.371	..	104.4 102.8	126 106	28 24
	12	1,845	0.992	1.645	0.464	..	104.4 102.0	124 110	26 24
	13	1,450	0.541	1.291	0.348	..	104.4 102.0	126 112	26 24
	14	1,600	0.625	1.318	0.372	..	104.0 100.8	120 100	20 20
	15	1,340	0.523	1.175	0.459	..	103.8 101.4	120 100	24 22
	16	1,660	0.651	1.568	0.510	..	104.0 101.0	124 100	24 24
	17	1,006	0.383	0.824	0.302	..	102.6 101.4	124 100	24 24
	18	2,135	0.918	1.524	0.312	48	102.8 101.0	116 100	24 24
	19	1,139	0.471	0.831	0.300	..	102.8 99.0	108 100	24 24
	20	1,740	0.401	1.242	0.411	..	102.0 99.8	104 96	24 24
	21	1,810	0.509	1.158	0.344	..	103.0 99.4	120 80	24 20
	22	1,270	0.438	1.055	0.320	..	102.0 99.6	112 92	24 24
	23	1,470	0.406	1.035	0.190	..	102.8 99.0	110 92	24 24
	24	2,320	0.489	1.192	0.520	..	102.6 99.0	112 99	24 22
	25	1,110	0.317	0.855	0.154	..	102.6 99.6	108 100	24 24
	26	1,245	0.311	0.871	0.125	..	101.0 98.6	100 96	24 24
	27	1,425	0.321	0.890	0.129	45	100.0 99.0	104 92	24 20
	28	1,505	0.341	0.873	0.106	..	100.0 98.6	108 84	24 24
	29	1,155	0.289	0.866	0.096	..	100.0 98.6	108 84	24 24
	30	1,405	0.332	0.897	0.080	..	99.6 98.4	96 92	24 20
	31	1,445	0.275	0.850	0.104	..	100.0 98.6	116 96	24 24
	32	1,285	0.305	0.881	0.063	..	99.8 98.0	100 88	24 24
	33	1,740	0.386	0.887	0.122	44	99.0 98.0	100 92	24 24
	34	1,065	0.472	0.902	0.063	..	99.8 99.0	100 92	24 24

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
3 (cont.)	35	1,580	0.342	0.585	0.000	..	99.0 97.8	94 92	24 24
	36	1,030	0.254	0.960	0.000	..	99.4 98.4	100 86	24 24
	37	1,155	0.328	0.962	0.000	..	99.4 98.4	100 84	24 24
4	1	.....	.....	.....	.....	58			
	3	1,260	0.433	0.764	0.270		101.0 100.0	108 96	28 24
	4	1,690	0.644	0.975	0.433	..	100.4 99.6	100 84	24 24
	5	920	0.465	0.534	0.239	..	100.0 99.5	104 84	24 20
	6	1,460	0.348	0.963	0.554	..	100.0 99.0	104 88	24 22
	7	1,640	0.263	1.077	0.423	..	100.0 99.0	102 88	24 24
	8	1,110	0.608	0.782	0.450	..	101.0 100.0	98 92	24 20
	9	1,430	0.595	1.021	0.722	53	101.0 100.0	108 92	28 24
	10	1,065	0.429	0.934	0.397	..	100.6 96.8	100 92	24 20
	11	1,230	0.425	1.025	0.256	..	100.0 99.4	108 96	24 22
	12	1,055	0.449	1.059	0.039	..	100.0 99.6	100 92	24 22
	13	635+	0.358+	0.635+	0.070+	..	100.0 98.0	100 88	24 20
	14	1,295	0.481	0.481	0.000	..	100.0 99.0	106 92	26 20
	15	1,075	0.546	0.895	0.000	53	100.0 98.6	100 92	24 20
	16	1,525	0.360	0.802	0.000	..	99.6 98.6	96 84	24 20
	17	1,645	0.382	1.096	0.000	..	100.0 98.0	92 80	20 20
	18	1,540	0.360	0.887	0.000	..	99.4 98.4	94 80	24 20
	19	1,350	0.235	0.860	0.000	..	99.0 97.6	88 72	22 20
	20	1,225	0.279	0.872	0.000	..	99.8 98.0	84 76	22 20
	21	1,565	0.290	0.972	0.000	..	100.0 98.0	92 84	24 20
	22	1,505	0.293	0.753	0.000	..	100.0 97.6	84 80	24 24
	23	1,040	0.213	0.732	0.000	..	99.4 98.4	84 80	24 24

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
4 (cont.)	24	1,600	0.345	0.896	0.000	55.5	99.0 98.0	100 80	24 24
	25	1,060+	0.138+	0.498	0.000	..	99.0 98.0	80 68	20 20
	26	2,090	0.359	0.836	0.000	..	99.0 98.0	84 80	22 20
	27	2,220	0.565	0.844	0.000	..	99.0 98.4	80 78	22 22
	28	1,980	0.300	0.891	0.000	..	99.0 97.6	84 80	24 20
	29	2,200	0.305	0.981	0.000	..	99.0 98.4	84 80	24 24
5	1	755	0.205	1.178	0.398	58	101.0 101.0	90 84	24 24
	2	970	0.694	1.178	0.398	..	101.0 99.0	108 96	30 24
	3	970	0.584	1.469	0.000	..	99.0 98.0	104 76	28 24
	4	825	0.584	0.998	0.148	..	99.0 97.0	88 64	24 24
	5	905	0.314	1.072	0.134	..	98.6 97.6	86 60	24 20
	6	980	0.524	1.063	0.127	57	98.6 97.0	86 60	24 20
	7	1,730	0.593	1.536	0.134	..	98.0 97.0	84 56	20 18
	8	1,025	0.391	0.977	0.113	..	98.6 97.0	84 56	20 18
	9	1,110	0.221	1.356	0.000	..	98.8 97.0	72 68	20 18
	10	1,200	0.314	1.000	0.000	..	98.8 97.4	68 56	22 20
	11	1,455	0.342	1.323	0.000	..	98.0 97.8	64 56	22 18
	12	1,440	0.314	0.986	0.000	..	98.6 97.6	70 60	20 18
	13	1,970	0.406	1.447	0.000	57	98.6 98.0	64 52	20 18
	14	5857	?	?	0.000	..	99.0 98.0	68 52	20 20
	15	lost	.....	.....	.....	..	99.4 98.6	64 60	20 18
	16	1,280	0.320	1.600	0.000	..	100.8 99.0	84 64	20 20
	17	885	0.278	1.106	0.000	..	100.6 98.6	88 80	20 20
	18	725	0.207	0.761	0.000	..	101.4 98.6	84 80	20 20
	19	5007	?	?	0.000	..	100.0 99.8	88 80	20 20

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
5 (cont.)	20	1,065	0.218	1.325	0.000	..	103.0 99.8	100 80	24 24
	21	640?	?	?	0.000	..	102.8 99.8	100 80	24 24
	22	1,165	0.422	1.354	0.000	..	101.6 99.8	112 84	24 24
	23	1,065	0.309	1.416	0.000	..	103.4 100.0	100 88	26 24
	24	595?	?	?	0.000	..	103.6 100.0	100 88	26 24
	25	965	0.296	1.231	0.000	..	103.0 99.0	108 80	24 24
	26	970	0.258	1.241	0.000	..	102.6 99.0	112 88	24 24
	27	795	0.222	0.897	0.000	57	100.6 99.0	100 76	24 24
6	1	.....	.....	.....	.....	55.5			
	2	1,435	0.382	1.195	.....	..	101.0 99.0	112 88	28 24
	3	1,000	0.286	1.428	.....	..	100.4 98.6	100 88	28 20
	4	1,225	0.316	1.286	.....	..	100.4 98.0	100 98	24 20
	5	1,710	0.414	1.485	0.000	..	100.6 99.0	100 88	24 20
	6	1,260	0.344	1.399	0.000	..	101.0 98.6	96 80	24 20
	7	1,355	0.343	1.693	0.000	..	100.8 97.0	96 80	30 20
	8	950	0.226	0.950	0.000	..	101.0 98.0	100 84	24 24
	9	845	0.218	1.082	0.000	..	100.0 98.8	96 80	26 20
	10	1,855	0.549	1.886	0.000	..	101.0 98.0	104 80	24 20
	11	1,200	0.374	1.132	0.000	55	101.0 97.4	116 80	24 20
	12	1,245	0.413	1.270	0.000	..	100.4 97.4	104 76	26 20
	13	1,590	0.374	1.272	0.000	..	100.4 97.6	104 84	26 20
	14	1,260	0.398	1.168	0.000	..	100.6 98.0	100 80	24 24
	15	1,435	0.495	1.121	0.184	..	100.0 99.0	92 84	24 20
	16	1,220	0.426	0.964	0.065	..	99.8 97.0	96 80	20 20

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum Temperature, F.	Maximum and Minimum Pulse	Maximum and Minimum Respiration
6 (cont.)	17	1,965	0.623	1.193	0.000	..	99.8 97.4	96 72	24 20
	18	1,490	0.709	1.550	0.000	..	99.6 97.0	84 74	22 20
	19	1,000	0.351	0.606	0.000	..	99.8 98.0	108 80	26 22
	20	1,185	0.624	0.823	0.000	..	100.6 98.0	96 76	24 24
	21	1,970	0.624	2.052	0.000	..	99.4 98.0	88 80	24 24
	22	2,095	0.468	1.300	0.052	..	99.4 97.6	92 76	24 24
	23	1,045	0.313	0.746	0.000	..	99.4 97.0	94 80	24 20
	24	2,315	0.650	1.928	0.000	..	99.0 98.0	100 76	24 20
	25	1,500	0.574	1.491	0.000	56.4	99.8 98.4	88 80	24 20
	26	2,030	0.498	1.326	0.000	..	100.6 98.0	80 64	24 20
	27	1,980	0.340	1.356	0.000	..	99.8 97.0	104 76	28 20
	28	1,845	0.442	1.229	0.000	..	99.4 97.0	100 76	24 20
	29	1,475	0.369	1.134	0.000	..	100.0 97.0	90 76	24 24
	30	2,110	0.511	1.319	0.000	..	98.0 97.0	80 74	24 20
	31	2,140	0.413	1.189	0.000	56.8	99.0 97.0	88 76	20 20
	32	1,530	0.370	1.233	0.000	..	99.0 97.4	84 76	24 20
	33	2,675	0.509	1.295	0.000	..	100.4 97.0	104 80	24 20
7	1	.....	.....	.....	.....	60.5			
	3	940	0.368	1.880	0.000	..	102.8 100.0	112 90	28 20
	4	300	0.125	0.624	0.000	..	102.0 100.0	116 104	28 22
	5	495	0.136	0.852	0.000	..	102.0 101.0	112 92	28 24
	6	535	0.214	1.027	0.160	..	102.6 99.0	120 88	30 22
	7	850	0.340	1.828	0.000	59	102.0 100.0	104 88	28 22
	8	630	0.265	0.958	0.000	..	102.6 100.4	112 96	28 20
	9	600	0.333	0.626	0.012	....	102.6 99.8	112 96	28 20

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
7 (cont.)	10	1,370	0.760	1.956	0.000	..	102.8 100.0	98 92	24 24
	11	895	0.497	1.395	0.000	..	103.0 100.0	100 92	28 24
	12	530	0.262	0.663	0.000	..	102.0 100.0	104 88	24 24
	13	1,315	0.644	1.879	0.000	..	102.0 99.4	104 92	28 24
	14	1,205	0.522	1.401	0.000	..	101.4 98.4	96 88	26 24
	15	1,860	0.791	1.281	0.000	..	102.4 99.0	92 80	24 24
	16	895	0.373	0.963	0.000	57	101.0 98.8	90 80	24 20
	17	1,260	0.531	1.679	0.000	..	101.0 98.0	100 98	26 24
	18	1,045	0.580	1.458	0.000	..	101.0 99.0	92 88	24 20
	19	820	0.480	1.040	0.000	57	100.4 98.6	92 76	28 20
	20	1,150	0.575	1.239	0.000	..	99.6 98.0	104 76	24 24
	21	1,235	0.413	1.107	0.000	..	100.0 98.4	90 80	24 24
	22	1,280	0.288	1.254	0.000	..	101.0 98.6	84 76	26 24
	23	2,195	0.442	1.462	0.000	..	100.0 99.0	90 76	28 24
	24	2,075	0.461	1.597	0.000	..	100.0 98.0	80 48	24 24
	25	1,740	0.435	1.390	0.000	..	100.0 98.4	88 76	24 20
	26	2,165	0.476	1.442	0.000	..	100.0 97.0	84 74	22 20
	27	1,430	0.358	1.191	0.000	..	99.6 98.0	96 80	20 20
	28	1,310	0.375	1.284	0.000	57	100.0 98.0	84 80	20 20
	29	1,230	0.377	1.168	0.000	..	100.0 97.8	82 80	22 22
	30	1,690	0.449	1.504	0.101	..	100.0 98.8	84 72	22 18
	31	1,690	0.436	1.301	0.000	..	100.0 98.0	92 72	20 20
	32	630	0.207	0.838	0.000	..	100.0 98.4	84 76	20 20
	33	1,115	0.297	1.035	0.000	..	99.4 98.6	80 64	20 18
8	2	.....	.....	.....	.....	56.4			

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
8 (cont.)	3	1,785	0.723	2.173	0.111	..	104.6 101.0	102 72	24 20
	4	890	0.494	1.711	0.000	..	103.8 100.0	108 80	24 20
	5	840	0.484	1.589	0.000	..	102.6 99.6	88 68	24 20
	6	1,505	0.849	1.273	0.071	..	101.0 99.0	84 68	20 20
	7	1,555	0.524	1.233	0.000	..	99.0 96.0	72 56	20 18
	8	1,220	0.437	1.220	0.000	51	99.0 97.4	74 64	20 18
	9	1,135	0.407	0.813	0.068	..	99.0 97.6	56 44	20 18
	10	1,715	0.408	1.271	0.000	..	98.0 97.4	68 56	20 18
	11	1,825	0.382	1.207	0.000	..	99.0 97.0	80 76	24 20
	12	1,980	0.384	1.253	0.000	..	98.6 97.0	56 46	20 18
	13	1,760	0.305	1.035	0.032	..	98.6 97.6	52 40	20 18
	14	1,530	0.319	1.247	0.000	..	99.0 97.0	60 48	20 16
	15	1,650	0.252	0.999	0.000	..	99.8 97.0	66 60	22 20
	16	1,490	0.322	1.418	0.000	..	98.6 97.0	68 60	22 20
	17	2,440	0.356	1.220	0.000	55.5	99.6 97.8	60 56	20 20
	18	1,605	0.337	1.203	0.000	..	98.6 97.6	76 52	20 20
	19	1,985	0.256	1.113	0.000	..	98.6 97.4	54 48	18 16
9	1	.....	.....	.....	.....	58			
	2	815	0.282	1.630	0.000	..	100.4 99.0	92 80	24 24
	3	725	0.305	1.450	0.000	..	102.8 100.0	100 80	26 24
	4	875	0.364	1.093	0.000	..	101.0 99.6	94 80	24 24
	5	1,250	0.363	1.662	0.000	..	100.0 98.0	92 76	24 24
	6	1,075	0.325	1.247	0.000	..	99.8 98.0	80 72	24 24
	7	960	0.307	1.449	0.000	..	99.4 98.4	80 64	24 24
	8	1,085	0.304	1.550	0.000	..	99.6 98.4	80 64	22 20

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
9 (cont.)	9	1,510	0.380	1.676	0.000	..	100.0 98.4	80 68	20 18
	10	1,020	0.271	1.132	0.000	..	102.0 98.8	80 64	24 24
	11	1,800	0.367	1.800	0.000	..	99.0 98.6	80 64	24 24
	12	1,520	0.328	1.520	0.000	58	99.4 98.6	80 64	24 24
	13	1,330	0.287	0.838	0.000	..	99.8 98.4	80 60	24 18
	14	1,500	0.302	1.363	0.000	..	99.0 98.0	80 72	24 24
	15	1,410	0.268	1.128	0.000	..	99.0 98.6	72 60	20 20
	16	1,120	0.198	1.018	0.000	..	99.4 98.4	72 64	20 20
	17	2,135	0.405	1.836	0.000	..	99.4 98.0	92 60	24 24
	18	1,475	0.319	1.287	0.000	..	98.8 98.0	80 72	24 24
	19	2,000	0.554	1.538	0.000	58	98.8 98.4	74 60	24 24
	20	800	0.262	0.809	0.000	..	99.8 98.4	74 60	24 24
	21	1,295	0.204	1.439	0.000	..	98.6 97.6	68 60	24 24
	22	1,655	0.320	1.798	0.000	..	98.6 98.0	72 72	24 24
	23	1,380	0.299	1.254	0.000	..	98.6 98.6	68 68	24 24
10	2	.....	.....	.....	.....	54			
	3	700	0.465	1.286	0.000	..	102.8 102.0	112 100	28 28
	4	735	0.282	1.049	0.118	..	103.0 100.8	112 100	28 28
	5	630	0.494	1.050	0.525	..	103.0 101.4	112 92	28 26
	6	490+	0.415+	0.650+	0.413+	..	103.0 101.6	110 96	28 26
	7	770	0.638	1.070	0.470	51	102.8 101.4	102 90	28 26
	8	500+	0.298+	0.741+	0.468+	..	102.6 100.6	108 100	28 28
	9	340+	0.291+	0.607+	0.364+	..	102.6 101.0	104 96	26 26
	10	710	1.665	1.291	0.577	..	102.6 100.6	108 100	28 28

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
11	2	.....	.....	.....	.....	48.6			
	9	.....	.....	.....	.....	45			
	11	820	0.455	0.960	0.000	..	102.6 100.0	112 96	26 26
	12	580	0.358	0.722	0.000	..	102.0 100.0	124 96	28 26
	13	660	0.421	0.812	0.000	..	102.4 100.0	112 88	30 26
	14	680	0.219	0.750	0.000	..	102.8 100.0	120 88	30 26
	15	605	?	0.756	0.000	..	103.0 100.0	132 100	44 30
	16	lost	.....	.....	.....	45	103.0 100.0	128 116	32 28
	17	740	0.440	0.967	0.000	..	103.0 102.0	132 112	40 32
	18	500	0.378	0.758	0.000	..	102.6 100.0	132 104	36 32
	19	980	0.628	0.859	0.000	..	103.6 100.4	132 108	32 28
	20	1,065	0.535	0.886	0.000	..	103.0 100.0	124 100	28 28
	21	540	?	0.540+	0.136+	..	103.4 99.0	124 116	28 28
	24	1,110	0.756	1.000	0.000	45	102.8 99.0	120 96	28 26
	25	1,120	0.612	0.855	0.000	..	102.0 100.0	110 88	26 24
	26	650	0.580	0.812	0.000	..	102.0 100.0	112 90	28 26
	28	900	0.562	0.900	0.000	..	102.0 99.8	104 96	28 28
12	2	.....	.....	.....	.....	26.4			
	7	955	0.273	0.542	0.139	..	102.0 97.8	116 80	24 24
	8	900	0.247	0.473	0.107	..	101.0 98.0	100 80	24 22
	9	905	0.237	0.362	0.045	27.7	99.0 98.4	96 80	24 24
	10	1,335	0.312	0.494	0.063	..	99.0 97.8	100 80	24 22
	11	1,800	0.298	0.465	0.037	..	99.0 98.4	92 98.4	24 22
	12	1,370	0.358	0.630	0.000	..	99.6 98.6	104 80	24 22
	13	1,580	0.262	0.600	0.000	..	99.6 98.6	88 80	22 20
	14	1,320	0.230	0.362	0.000	..	100.0 98.6	112 80	24 20

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
12 (cont.)	15	1,355	0.190	0.501	0.000	..	102.0 99.0	124 80	28 20
	16	1,745	0.454	0.820	0.000	..	103.8 100.8	132 108	20 24
	17	770+	?	?	0.039+	..	104.4 102.0	144 100	28 24
	18	680+	?	?	0.126+	31.8	103.6 101.6	128 104	30 24
	19	1,035	0.228	0.517	0.053	..	104.0 102.0	128 92	30 24
	20	1,165	0.238	0.641	0.128	..	103.4 100.6	126 108	24 24
	21	Lost	.....	.....	.....	..	103.0 98.4	120 92	24 24
	22	1,335	0.254	0.668	0.260	..	102.0 98.6	124 92	24 24
	23	1,245	0.187	0.401	0.187	..	101.0 97.8	104 90	24 24
	24	1,255	0.196	0.402	0.100	..	100.8 97.4	88 80	24 24
	25	1,285	0.276	0.510	0.086	29	100.0 97.4	92 84	24 24
	26	1,375	0.261	0.491	0.000	..	98.6 97.4	80 88	24 24
	27	810	?	0.336	0.046	..	99.0 97.4	88 80	24 24
	28	1,235	0.152	0.449	0.055	..	98.8 97.8	84 68	24 24
	29	1,535	0.307	0.421	0.045	..	98.6 97.8	84 76	24 24
	30	1,385	0.204	0.449	0.023	..	98.6 97.6	80 72	24 24
	31	1,355	0.194	0.386	0.000	..	99.0 98.0	96 92	24 24
	32	875	?	0.355	0.000	..	98.6 98.4	84 80	24 24
	33	1,355	0.329	0.430	0.040	30	98.6 98.0	84 80	24 24
	34	1,530	0.318	0.424	0.071	..	99.0 97.8	88 80	24 24
	35	1,010	0.509	0.323	0.064	..	98.6 97.6	84 80	24 24
	36	1,505	0.295	0.470	0.061	..	98.6 98.4	96 76	24 24
	37	1,020	0.265	0.409	0.057	..	101.0 98.0	88 80	24 24
	39	.....	.....	.....	.....	31.4			

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
13	1	.....	.....	.....	.....	56			
	2	1,215	0.530	1.276	0.547	..	104.0 100.6	128 104	48 36
	3	1,420	0.861	1.291	0.982	..	105.0 102.8	132 120	32 28
	4	1,410	0.989	1.282	0.792	..	128.0 88.0	128 88	30 20
	5	1,170	0.779	1.004	0.692	..	101.0 99.8	102 76	30 26
	6	1,110	0.778	1.232	0.899	..	100.8 99.0	100 72	30 22
	7	770	0.494	1.009	0.650	..	99.8 99.0	96 60	32 24
	8	1,185	0.498	1.148	1.097	..	99.8 98.6	68 60	28 20
	9	800	0.722	1.269	0.666	..	100.0 98.0	80 64	24 20
	10	920	0.767	1.045	0.737	51.8	99.0 98.6	76 60	24 20
	11	650	0.591	0.764	0.319	..	99.0 97.8	88 56	28 20
	12	1,220	0.813	1.106	0.855	..	100.6 98.0	70 56	24 20
	13	820	0.462	0.966	0.248	..	99.0 97.0	72 60	24 20
	14	555+	?	0.673+	0.318+	..	99.0 97.0	60 44	20 20
	15	850	0.488	1.307	0.000	..	98.8 97.0	70 50	24 18
	16	905	0.529	0.983	0.148	..	98.6 97.0	62 62	20 18
	17	1,185	0.327	0.912	0.000	52.3	99.0 97.8	52 48	20 20
	18	1,050	0.317	1.050	0.000	..	99.0 97.6	70 56	22 18
	19	1,405	0.434	1.151	0.000	..	99.4 97.0	70 52	20 18
	20	735	0.196	0.816	0.000	..	99.4 98.0	76 60	24 20
	21	940	0.290	1.147	0.000	..	100.0 97.8	76 60	20 20
	22	1,245	0.384	1.132	0.000	..	99.4 97.6	76 60	20 20
	23	985	0.371	1.034	0.000	..	99.0 97.8	76 60	20 20
	24	1,430	0.298	0.916	0.000	55.5	99.0 97.6	72 60	20 18

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
14	1	.....	.....	.....	.....	55.5			
	2	1,140	0.414	0.950	0.095	..	99.8 97.8	80 60	30 20
	3	1,150	0.460	0.756	0.337	..	98.6 97.6	68 52	20 18
	4	2,765	1.136	1.535	0.539	..	98.4 97.8	80 56	20 18
	5	1,970	0.636	1.037	0.412	..	102.6 97.8	86 52	24 20
	6	1,935	0.549	1.105	0.482	..	98.0 97.6	64 48	22 18
	7	1,850	0.508	1.265	0.301	..	98.6 98.0	64 52	22 18
	8	1,845	0.481	1.164	0.302	..	98.6 97.8	60 52	20 16
	9	2,025	0.810	1.841	0.409	..	98.0 97.0	72 50	22 18
	10	1,320	0.419	1.145	0.175	..	98.6 98.0	62 60	20 20
	11	1,520	0.496	1.408	0.000	52.3	99.4 98.0	60 52	20 18
	12	2,115	0.589	1.438	0.000	..	99.0 97.0	60 46	20 16
	13	1,250	0.356	0.951	0.185	..	98.6 97.0	72 50	20 18
	14	1,845	0.419	1.317	0.124	52.3	99.0 97.6	62 44	24 18
	15	1,310	0.304	0.872	0.097	..	99.0 98.0	52 46	20 18
	16	1,715	0.408	1.271	0.000	..	99.0 97.0	52 46	18 18
	17	1,825	0.416	1.293	0.000	..	98.6 97.4	60 52	22 18
	18	1,575	0.295	1.125	0.000	..	98.6 97.0	52 44	20 18
	19	1,885	0.346	1.327	0.000	..	99.0 97.0	52 50	18 18
	20	1,435	0.276	1.879	0.000	..	98.8 97.0	60 52	18 18
15	2	1,285	0.702	1.799	0.257	54.5	104.0 102.6	112 100	32 30
	3	1,110	0.670	1.354	0.000	..	102.4 97.0	104 72	30 26
	4	1,090	0.519	0.894	0.000	..	98.6 97.0	84 72	26 20
	5	720	0.281	0.621	0.000	..	100.0 97.0	84 56	26 20
	6	1,210	0.332	0.932	0.000	..	98.6 98.4	84 52	28 24

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Creatinin in Gm.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
15 (cont.)	7	1,500	0.262	1.102	0.000	..	98.0 96.0	72 60	24 24
	8	985	0.302	0.982	0.000	53	99.0 97.0	72 60	24 24
	9	820	0.248	0.861	0.000	..	100.0 97.0	72 52	24 20
16	1	.....	.....	.....	.....	56.4			
	14	.....	.....	.....	.....	49.5			
	24	.....	.....	.....	.....	48			
	27	1,920	0.545	0.730	0.101	..	99.4 98.4	88 72	24 20
	28	2,210	0.544	0.914	0.136	..	99.0 97.6	84 64	24 22
	29	1,575	0.387	0.606	0.051	..	98.6 96.0	84 66	22 22
	30	2,130	0.609	0.805	0.000	..	99.0 97.6	84 66	20 20
	31	1,805	0.451	0.704	0.000	..	99.0 97.8	80 74	20 20
	32	1,410	0.329	0.671	0.000	45.4	98.8 97.0	80 68	20 20
	33	2,125	0.497	0.748	0.000	..	99.4 98.0	80 66	20 20
	34	1,860	0.495	0.874	0.000	..	99.4 97.8	70 60	20 18
	35	2,105	0.493	0.956	0.000	..	99.6 98.0	72 56	20 20
	36	1,335	0.296	0.621	0.000	..	99.4 97.4	68 52	20 18
	37	1,995	0.407	0.866	0.000	..	100.0 98.6	76 64	20 18
	38	2,225	0.387	0.934	0.000	..	100.0 98.6	76 72	22 20
	39	2,250	0.392	0.843	0.000	48	99.0 98.4	72 56	20 18
	40	1,900	0.370	0.915	0.000	..	99.0 99.0	72 56	20 20
				Gm. of P_2O_5 Excreted in 24 Hrs.					
17	10	2,050	0.957	.....	.....	..	100.0 98.0	90 80	
	11	1,440	0.655	2.475	.....	58	100.0 98.6	80 75	
	12	1,540	0.762	2.883	.....	..	99.0 98.0	80 60	
	13	1,420	0.551	2.623	.....	..	99.0 98.0	70 60	

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Gm. of P_2O_5 Excreted in 24 Hrs.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
17 (cont.)	14	1,610	0.806	3.274	.....	..	99.0 97.0	70 60	
	15	1,390	0.610	2.312	.....	..	99.0 97.0	80 60	
	16	1,570	0.618	2.450	.....	..	99.0 98.0	80 70	
	17	1,460	0.658	2.686	.....	..	99.6 97.6	90 60	
	18	1,205	0.385	2.217	.....	57	99.0 97.4	75 65	
	19	1,810	0.601	2.329	.....	..	98.6 97.0	90 60	
	20	1,565	0.623	. ...	.....	..	102.4 97.0	110 70	
	21	1,565	0.623	2.054	.....	..	104.4 102.4	120 100	
	22	2,370	0.562	3.381	.....	..	101.0 98.6	100 80	
	23	2,000	0.564	1.288	.....	57	98.8 98.0	85 60	
	24	655	0.328	1.065	.....	..	99.6 97.0	70 60	
	25	1,970	0.656	2.170	.....	..	99.8 98.0	85 70	
	26	2,885	0.481	4.877	.....	..	99.0 97.6	80 70	
	27	2,200	0.411	1.872	.....	..	99.4 97.4	85 70	
	28	3,000	0.458	1.552	.....	..	99.0 97.0	80 60	
	29	2,430	0.463	1.257	.....	..	98.6 97.8	80 60	
	30	1,915	0.471	2.288	.. ..	53.5	99.0 97.0	80 70	
	31	Lost							
	32	2,585	0.512	3.068	.....	..	99.0 97.0	80 60	
	33	1,775	0.384	2.530	.....	..	98.8 97.0	65 60	
	34	1,980	0.390	.....	.....	..	99.4 97.0	80 65	
	35	2,165	0.413	.....	.....	56	98.6 97.0	80 70	
	36	1,615	0.306	.....	.....	..	99.4 97.0	85 65	
	37	1,975	0.362	.....	.....	..	99.0 97.0	80 70	
	38	1,930	0.351	.....	.....	..	99.0 97.0	80 60	

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Gm. of P_2O_5 Excreted in 24 Hrs.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		Respiration
							Temperature, F.	Pulse	
18	10	900	0.681	0.353	.....	..	102.6 99.6	95 75	
	11	1,000	0.579	1.020	.....	64.5	102.0 100.6	100 80	
	12	540	0.338	0.412	.....	..	101.4 100.0	100 80	
	13	770	0.513	1.245	.....	..	101.4 99.4	100 90	
	14	570	0.456	0.668	.....	..	102.0 100.0	90 75	
	15	850	0.566	1.172	.....	..	102.4 100.0	95 70	
	16	760	0.528	1.258	.....	..	102.4 101.0	98 70	
	17	450	0.322	1.071	.....	..	102.4 100.0	85 70	
	18	500	0.410	0.920	.....	..	102.0 100.0	85 75	
	19	680	0.485	1.080	.....	..	101.0 98.0	90 65	
	20	1,000	0.708	1.112	.....	64.5	101.0 99.4	100 65	
	21	850	0.506	.....	.....	..	101.4 99.0	80 60	
	22	850	0.50[illegible]	1.236	.....	..	100.0 98.0	70 60	
	23	1,430	0.681	1.511	.....	..	98.8 97.0	70 55	
	24	1,570	0.800	1.209	.....	..	98.6 97.0	80 55	
	25	1,180	0.625	.....	.....	..	98.8 97.0	70 55	
	26	1,900	0.819	1.923	.....	..	98.6 98.0	70 60	
	27	2,985	0.670	1.470	.....	..	98.0 97.6	70 60	
	28	2,530	0.582	2.152	.....	..	98.6 97.6	80 60	
	29	3,770	0.710	1.548	.....	68	99.0 97.4	95 55	
	30	2,520	0.536	1.305	.....	..	98.6 97.0	75 60	
	31	1,565	0.425	2.265	.....	..	98.0 97.6	70 55	
	32	1,065	0.516	2.186	.....	..	97.8 97.0	90 55	
	33	1,740	0.442	.....	.....	..	97.6 97.0	65 55	

URINARY CREATIN, CREATININ, AND URIC ACID IN FEVERS—(*Continued*)

Case No.	Day in Hospital	Amount of Urine in 24 Hrs. in C.c.	Uric Acid in Gm.	Gm. of P_2O_5 Excreted in 24 Hrs.	Creatin in Gm.	Weight in Kg.	Maximum and Minimum		
							Temperature, F.	Pulse	Respiration
18 (cont.)	34	1,305	0.235	.....	.....	..	98.0 97.0	75 55	
	35	1,380	0.391	.....	.....	..	98.4 97.0	85 60	
	36	1,435	0.336	.....	.....	62	98.0 97.0	100 60	
	37	1,020	0.213	.....	.....	..	98.6 97.0	70 60	
	38	2,085	0.413	.....	.....	..	98.6 97.0	70 60	
	39	1,185	0.291	.....	.....	..	97.4 97.0	80 60	
	43	.....	.....	.....	.....	64			

THE COMPARATIVE FOOD VALUE OF PROTEIN, FAT AND ALCOHOL IN DIABETES MELLITUS AS MEASURED BY THE NITROGEN EQUILIBRIUM *

HERMAN O. MOSENTHAL, M.D.
AND
GEORGE A. HARROP, JR., M.D.
BALTIMORE

In a previous publication[1] it was claimed that probably the lowest diet which will conserve the physical and mental efficiency of the diabetic is that which maintains the nitrogen equilibrium of the patient. The experiments reported at that time showed that on a so-called carbohydrate-free diet, in which the proteins and fat were approximately equal to each other, gram for gram, maintenance, as measured by the nitrogen balance, was obtained at from 1,500 to 2,000 calories, the variations usually depending on the size and the sex of the patient. No attempts were made to determine which of the ingredients of a starch-free dietary, fat, protein or alcohol, was the most efficient protein sparer. In order to administer a diet of as low caloric value as possible, and still establish maintenance, it is essential to have this information.

The aim of the present investigation is to determine the comparative value of protein, fat and alcohol as nitrogen sparers, when added to the "carbohydrate-free" diet in diabetes mellitus. The patients observed were given diets of a constant protein, fat and starch content, and of such caloric value that there was a negative nitrogen balance. The fats and proteins were approximately equal to each other, gram for gram; the carbohydrates were those unavoidably present in the green vegetables. This constituted the control period; it was usually kept up for six days. Subsequently, definite amounts of protein, fat and alcohol were added to the dietary, and the effect on the nitrogen balance noted. The methods were the same as previously employed.[1] One of the experiments is presented in detail in Table 1. All the other cases were studied by similar methods, but only a summary of the findings is given in Tables 2 and 3.

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* From the Medical Clinic of The Johns Hopkins Hospital.

1. Mosenthal, H. O., and Clausen, S. W.: THE ARCHIVES INT. MED., 1918, **21,** 269.

TABLE 1.—Detailed Data from the Observations on a Case of Diabetes Mellitus, Male, Aged 47, Height, 177 Cm. This Is an Example of the Experiments as Carried Out in Each of the Cases, a Summary Only Being Presented in Tables 2 and 3

Date	Urine			Feces Nitrogen, Gm.	N Output, Gm.	N Intake, Gm.	N Balance, Gm.	Food, Gm.*				Calories			Weight, Kg.
	Glucose, Gm.	Acetone Bodies as B-oxy, Gm.	Nitrogen, Gm.					Protein	Fat	Carbohydrate	Alcohol	Total	Per Kg. per Day	Per Sq. M. per Hour	
4/ 2/18	0	9.03	10.08	1.42	11.50	11.50	0	71.9	70.3	12.7	0	1,001	19.3	25.6	51.9
4/ 3/18	0	20.57	12.57	1.42	13.99	11.42	−2.57	71.4	70.5	12.6	0	1,000	18.9	25.3	52.9
4/ 4/18	0	19.46	10.25	1.42	11.67	11.47	−0.20	71.7	70.3	12.7	0	1,000	18.7	25.1	53.6
4/ 5/18	0	25.74	17.03	1.42	18.45	11.46	−6.99	71.6	70.4	12.6	0	1,000	19.0	25.4	52.5
4/ 6/18	0	20.91	12.94	1.42	14.36	11.47	−2.89	71.7	70.2	12.9	0	1,000	19.2	25.3	52.0
4/ 7/18	0	13.01	12.57	1.42	13.99	11.41	−2.58	71.3	70.7	12.3	0	1,000	19.6	24.1	50.9
4/ 8/18	0	16.20	11.52	2.73	14.25	11.50	−2.75	71.9	70.4	12.3	71.4	1,500	29.4	38.7	51.0
4/ 9/18	0	8.50	11.22	2.73	13.95	11.39	−2.56	71.2	70.8	12.2	71.4	1,500	29.7	38.5	50.5
4/10/18	0	11.00	10.14	2.73	12.87	11.47	−1.40	71.7	70.3	12.6	71.4	1,499	29.6	38.5	50.6
4/11/18	0	8.65	12.00	2.73	15.33	11.46	−3.87	71.6	70.4	12.7	71.4	1,500	30.4	39.2	49.3
4/12/18	0	6.40	7.68	2.73	10.36	11.46	+1.10	71.6	70.5	12.3	71.4	1,499	30.8	39.8	48.7
4/13/18	0	6.19	10.76	2.73	13.49	11.41	−2.08	71.3	70.8	12.2	71.4	1,501	30.0	39.0	50.0
4/14/18	0	4.39	9.52	1.99	11.51	11.36	−0.15	71.0	**125.1**	12.1	0	1,504	30.3	39.3	49.5
4/15/18	0	6.79	12.10	1.99	14.09	11.36	−2.73	71.0	**125.0**	12.0	0	1,503	30.1	39.0	49.9
4/16/18	0	6.85	10.74	1.99	12.73	11.36	−1.37	71.0	**125.4**	12.0	0	1,507	30.7	39.4	49.1
4/17/18	0	6.04	11.36	1.99	13.35	11.38	−1.97	71.1	**125.2**	12.0	0	1,505	31.2	39.6	48.8
4/18/18	0	5.29	11.39	1.99	13.38	11.38	−2.00	71.1	**125.1**	12.0	0	1,504	30.8	39.9	48.7
4/19/18	0	7.88	13.95	1.99	15.94	11.39	−4.55	71.2	**125.0**	12.1	0	1,504	30.6	39.3	49.2
4/20/18	0	8.40	13.95	2.66	16.61	24.00	+7.39	**150.0**	89.2	13.3	0	1,499	31.1	39.6	48.7
4/21/18	0	10.98	14.65	2.66	17.31	24.02	+6.71	**150.1**	89.3	13.4	0	1,501	31.0	39.6	48.4
4/22/18	0	5.05	11.97	2.66	14.63	24.05	+9.42	**150.3**	89.1	13.3	0	1,499	31.2	39.6	48.0
4/23/18	0	8.17	12.58	2.66	15.24	24.02	+8.78	**150.1**	89.4	13.1	0	1,501	30.7	39.9	48.7
4/24/18	0	9.33	11.29	2.66	13.95	24.02	+10.07	**150.1**	89.4	13.2	0	1,501	31.3	39.7	47.9
4/25/18	0	5.67	11.09	2.66	13.75	24.02	+10.27	**150.1**	89.5	13.1	0	1,502	30.1	39.9	48.7

* The articles of food printed in heavy type indicate the addition to the control diet.

TABLE 2.—Condensed Data from Cases of Diabetes Mellitus on Carbohydrate-Free Diets, Showing the Comparative Value of Protein, Fat and Alcohol as Nitrogen Sparers. The Daily Food Was Constant During Each Period

Patient	Period-Days	Glycosuria, Gm. per Day	Nitrogen, Gm. per Day			Food, Gm. per Day *				Calories			Acetone Bodies in Urine as B-oxy., Gm. per Day
			Intake	Output (Urine and Feces)	Balance	Protein	Fat	Carbohydrate	Alcohol	Total per Day	Per Kilo per Day	Per Sq. M. per Hour	
Case 1 Medical History No. 39566 Male, aged 68 Height, 170 cm. (5 ft. 7 in.) Weight, 70 kg. (154 lbs.)	6	0	11.4	14.2	−2.8	71.4	70.5	12.3	0	999	14.3	23.0	12.7
	6	0	11.4	14.4	−3.0	71.5	70.4	12.4	71.4	1,499	21.4	34.5	12.7
	6	0	11.4	11.9	−0.5	71.3	125.1	12.1	0	1,505	21.5	34.7	8.0
	6	0	11.5	12.4	−0.9	71.7	70.6	12.4	0	1,001	14.3	23.0	9.4
	6	0	11.4	13.7	−2.3	71.1	125.2	12.1	0	1,506	21.5	34.7	9.9
	6	0	11.4	13.9	−2.5	71.4	70.5	12.4	71.4	1,499	21.4	34.5	10.5
	6	0	24.1	18.3	+5.8	150.3	89.3	13.5	0	1,502	21.5	34.6	9.8
Case 2 Medical History No. 39586 Male, aged 47 Height, 177 cm. (5 ft 10 in.) Weight, 50 kg. (110 lbs.)	6	0	11.5	14.0	−2.5	71.6	70.4	12.6	0	1,000	20.0	25.8	18.1
	6	0	11.4	13.4	−2.0	71.5	70.5	12.4	71.4	1,499	30.0	38.7	9.5
	6	0	11.4	13.5	−2.1	71.1	125.2	12.0	0	1,505	30.1	38.8	6.2
	6	0	24.0	15.3	+8.7	150.1	89.3	13.2	0	1,500	30.0	38.7	7.9
Case 3 Medical History No. 39300 Male, aged 22 Height, 172 cm. (5 ft. 8 in.) Weight, 52 kg. (114 lbs.)	6	0	11.4	14.4	−3.0	71.5	70.5	12.4	0	1,000	19.2	25.9	
	6	0	11.5	13.8	−2.3	71.6	70.5	12.5	71.4	1,500	28.9	38.9	8.8
	6	0	11.4	14.3	−2.9	71.4	125.2	12.2	0	1,507	29.0	39.0	7.2
	6	0	11.4	12.7	−1.3	71.5	70.4	12.8	0	1,000	19.2	25.9	9.9
	6	0	24.0	25.1	−1.1	150.2	143.2	13.3	0	2,002	38.5	51.9	9.3
	6	0	24.1	24.9	−0.8	150.4	143.2	25.3	0	2,052	39.5	53.2	11.2
Case 4 Medical History No. 38448 Male, aged 33 Height, 177 cm. (5 ft. 10 in.) Weight, 60 kg. (132 lbs.)	6	0	11.5	12.1	−0.6	71.6	70.5	12.5	0	1,000	16.7	23.9	
	6	0	11.4	13.3	−1.9	71.5	70.4	12.4	71.4	1,499	25.0	35.8	10.2
	6	0	11.4	12.9	−1.5	71.2	125.2	12.1	0	1,506	25.1	36.0	8.8
	6	0	24.0	19.1	+4.9	150.2	89.2	13.5	0	1,501	25.0	35.8	12.3

Case 5 Medical History No. 39079 Male, aged 59 Height, 168 cm. (5 ft. 4 in.) Weight, 47 kg. (103 lbs.)	3	0	11.6	14.3	−2.7	72.2	70.2	12.2	0	999	21.3	28.1	
	6	0	11.6	13.3	−1.7	72.5	70.2	12.4	37.6	1,264	26.9	35.5	
	6	0	11.6	13.3	−1.7	72.2	70.3	12.1	0	999	21.3	28.1	
	6	0	11.4	10.2	+1.2	71.3	125.4	12.1	0	1,508	32.1	42.4	
	6	0	11.4	11.9	−0.5	71.4	125.3	12.6	37.6	1,773	37.7	49.8	
	6	0	24.0	18.4	+5.6	150.2	89.4	13.1	0	1,501	31.9	42.2	
	6	0	11.5	14.9	−3.4	71.7	70.3	12.5	37.6	1,262	26.9	35.5	
	6	0	11.4	12.1	−0.7	71.2	125.1	12.1	0	1,506	32.0	42.3	
	6	0	11.4	12.5	−1.1	71.3	70.4	12.8	0	1,000	21.3	28.1	
	6	0	24.1	21.5	+2.6	150.6	89.2	13.4	0	1,502	32.0	42.2	
	6	0	11.4	14.5	−3.1	71.2	125.2	12.1	0	1,506	32.0	42.3	
	6	0	11.5	13.7	−2.2	71.6	70.4	12.3	71.4	1,499	31.9	42.1	
	6	0	11.4	12.3	−0.9	71.2	125.2	12.2	71.4	2,006	42.7	56.4	
Case 6 Medical History No. 39254 Male, aged 55 Height, 173 cm. (5 ft. 8 in.) Weight, 56 kg. (123 lbs.)	6	0	11.4	14.4	−3.0	71.5	70.5	12.4	0	1,000	17.9	25.0	
	6	0	11.5	13.8	−2.3	71.6	70.5	12.5	71.4	1,500	26.8	37.5	
	6	0	11.4	14.3	−2.9	71.4	125.2	12.2	0	1,507	26.9	37.7	
	6	0	11.4	12.7	−1.3	71.5	70.4	12.8	0	1,000	17.9	25.0	
	6	0	11.4	13.7	−2.3	71.2	125.3	12.4	0	1,508	26.9	37.7	
	6	0	11.5	14.2	−2.7	71.6	70.5	12.5	71.4	1,500	26.8	37.5	
	8	0	24.0	20.3	+3.7	150.1	89.3	13.3	0	1,500	26.8	37.5	
	6	0	24.0	24.6	−0.6	150.1	89.5	13.3	35.5	1,751	31.3	43.8	
	6	0	24.0	21.2	+2.8	150.1	118.2	13.2	0	1,750	31.3	43.7	
Case 7 Medical History No. 39176 Male, aged 23 Height, 167 cm. (5 ft. 6 in.) Weight, 40 kg. (88 lbs.)	8	0	11.5	14.4	−2.9	71.8	70.4	12.5	0	1,000	25.0	29.6	
	6	0	11.4	11.9	−0.5	71.5	70.5	12.6	71.4	1,500	37.5	44.4	
	6	0	11.4	10.2	+1.2	71.2	126.8	12.4	0	1,520	38.0	45.0	
	6	12.0	11.5	12.4	−0.9	71.6	70.6	12.5	0	1,001	25.0	29.6	
	4	7.0	11.4	9.7	+1.7	71.4	125.4	12.2	0	1,509	37.7	44.6	

* The articles of food printed in heavy type indicate the addition to the control diet.

TABLE 2.—Condensed Data from Cases of Diabetes Mellitus on Carbohydrate-Free Diets, Showing the Comparative Value of Protein, Fat and Alcohol as Nitrogen Sparers. The Daily Food Was Constant During Each Period—(*Continued*)

Patient	Period-Days	Glycosuria, Gm. per Day	Nitrogen, Gm. per Day			Food, Gm. per Day *				Calories			Acetone Bodies in Urine as B-oxy., Gm. per Day
			Intake	Output (Urine and Feces)	Balance	Protein	Fat	Carbohydrate	Alcohol	Total per Day	Per Kilo per Day	Per Sq. M. per Hour	
Case 8 Medical History No. 38000 Male, aged 35 Height, 156 cm. (5 ft. 2 in) Weight, 43 kg. (95 lbs.)	7	0	11.5	13.0	−1.5	71.9	70.2	12.1	0	997	23.2	29.7	
	7	0	11.4	14.3	−2.9	71.4	70.7	12.2	37.6	1,363	29.4	37.6	
	6	0	11.4	12.7	−1.3	71.3	125.4	12.4	0	1,509	35.1	44.9	
	6	0	24.1	18.0	+6.1	150.3	69.7	13.3	0	1,505	35.0	44.8	
	6	0	11.4	13.1	−1.7	71.5	70.3	12.5	37.6	1,361	29.3	37.6	
	6	0	11.5	11.3	+0.2	71.6	70.4	12.4	0	999	23.2	29.7	
	6	0	24.0	18.3	+5.7	150.2	69.4	13.5	0	1,503	35.0	44.8	
	4	0	11.4	14.8	−3.4	71.4	125.6	12.0	0	1,510	35.1	44.9	
Case 9 Medical History No. 38696 Male, aged 52 Height, 169 cm. (5 ft. 7 in.) Weight, 44 kg. (97 lbs.)	8	0	11.7	12.8	−1.1	73.2	70.4	10.8	0	1,000	22.7	28.2	
	8	0	11.5	13.3	−1.8	71.8	70.4	12.3	37.6	1,263	28.7	35.6	
	3	0	11.4	12.9	−1.5	71.2	70.3	12.3	0	996	22.6	28.1	
	6	0	11.6	12.4	−0.8	72.4	70.2	12.4	37.6	1,264	28.7	35.6	
	6	0	11.6	12.4	−0.8	72.3	70.4	12.2	0	1,001	22.8	28.2	
	6	0	11.4	12.4	−1.0	71.1	125.3	11.9	0	1,506	34.2	42.4	
	6	0	24.0	19.0	+5.0	150.2	69.8	12.0	0	1,500	34.1	42.3	

Case 10 Medical History No. 39619 Male, aged 49 Height, 162 cm. (5 ft. 4 in.) Weight, 59 kg. (130 lbs.)	6	0	16.9	20.8	−3.9	105.7	105.7	20.6	0	1,501	25.4	38.5	15.9
	6	0	22.1	27.1	+5.0	**200.3**	117.7	20.5	0	2,000	33.9	51.3	8.9
	6	0	16.9	19.9	−3.0	105.6	105.7	20.5	71.4	2,000	33.9	51.3	7.5
	6	0	22.1	23.7	+8.4	**200.4**	117.6	20.9	0	2,001	33.9	51.3	13.2
	6	0	22.1	26.8	+5.3	**200.6**	117.5	20.7	0	2,000	33.9	51.3	18.8
	6	0	22.1	24.5	+7.6	**200.7**	117.6	20.5	0	2,001	33.9	51.3	6.0
	9	0	22.1	25.4	+6.7	**200.5**	117.6	20.5	0	2,000	33.9	51.3	8.2
Case 11 Medical History No. 39618 Male, aged 25 Height, 176 cm. (5 ft. 9 in.) Weight, 72 kg. (158 lbs.)	6	0	11.4	14.4	−3.0	71.3	70.6	12.5	0	1,000	13.9	22.2	
	6	0	24.1	19.5	+4.6	**150.3**	89.2	13.2	0	1,500	20.8	33.3	
	6	0	24.1	19.0	+5.1	**150.6**	89.1	13.3	0	1,501	20.8	33.3	13.78
	6	0	24.0	22.1	+1.9	**150.1**	89.2	13.5	0	1,500	20.8	33.3	17.05
	6	0	24.0	23.4	+0.6	**150.2**	89.3	13.2	0	1,500	2.08	33.3	10.01
	9	0	24.0	25.3	−1.3	**150.2**	89.3	13.2	0	1,500	2.08	33.3	9.47
Case 12 Medical History No. 39660 Male, aged 26 Height, 167 cm. (5 ft. 6 in.) Weight, 66 kg. (145 lbs.)	6	0	11.4	15.0	−3.6	71.3	70.5	12.5	0	999	15.1	23.9	
	6	0	11.4	14.3	−2.9	71.2	**125.2**	12.1	0	1,506	22.8	36.0	
	6	0	24.0	20.0	+4.0	**150.1**	89.6	12.9	0	1,502	22.8	35.9	
Case 13 Medical History No. 39820 Male, aged 33 Height, 169 cm. (5 ft 7 in.) Weight, 53 kg. (117 lbs.)	6	0	11.5	10.2	+1.3	71.6	70.6	12.7	0	1,002	18.9	26.1	9.5
	6	0	24.0	19.3	+4.7	**150.1**	89.6	13.2	0	1,503	28.4	39.1	10.2
Case 14 Medical History No. 39182 Male, aged 44 Height, 179 cm. (5 ft 10 in) Weight, 42 kg. (92 lbs.)	6	2.8	11.2	12.7	−1.5	69.7	**112.7**	9.3	**38.7**	1,643	39.1	45.3	
	6	26.8	21.6	22.2	−0.6	**135.2**	76.1	9.9	**38.7**	1,574	37.5	43.3	

* The articles of food printed in heavy type indicate the addition to the control diet.

TABLE 3.—Summary of Table 2, Giving the Average Daily Nitrogen Balance in Grams During the Different Periods of Feeding

Case No.	Character of Period						
	Control	Protein	Fat	Alcohol	Protein Plus Fat	Fat Plus Alcohol	Protein Plus Alcohol
1	−1.9	+5.8	−1.4	−2.8			
2	−2.5	+3.7	−2.1	−2.0			
3	−2.2	.....	−2.9	−2.3	−1.0		
4	−0.6	+4.9	−1.5	−1.9			
5	−1.8	+4.1	−0.9	−2.4	.....	−0.7	
6	−2.2	+3.7	−2.0	−2.5	+2.8	.....	−0.6
7	−1.9	.....	+1.5	−0.5			
8	−0.7	+5.9	−2.4	−2.3			
9	−1.1	+5.0	−1.0	−1.3			
10	−3.9	+6.0	.....	−3.0			
11	−3.0	+2.5					
12	−3.6	+4.0	−2.9				
13	+1.3	+4.7					
14	.....	.....	.....	.....	.....	−1.5	−0.6

It is evident from a study of these tables that fat and alcohol, when added to a low caloric protein-fat diet, have little or no influence in sparing nitrogen; protein, however, has a very positive influence in this regard. These findings are not absolutely constant in all these observations. Thus, Case 7 has a distinct retention of nitrogen during the high fat feeding and Case 5 (Table 2) exhibits the same phenomenon in the first of the three fat periods, but not in the two subsequent ones. There was no exception to the rule that alcohol was of no value as a nitrogen sparer, even when it was combined with protein, as in Cases 6 and 14, or with fat, as in Cases 5 and 14. With one exception, during a combined fat and protein period in Case 3, there was marked retention of nitrogen when a high protein diet was used, and even in the one instance cited there was a diminished loss of nitrogen, as compared to the control figures.

Lusk,[2] quoting the work of Thomas and Rubner, shows how the body may maintain nitrogen equilibrium much more readily on a protein-fat diet than on one of protein alone, and how with increasing quantities of fat there is an increasing addition of protein to the body. In the present experiments, the latter statement has proved itself to be

2. Lusk, G.: The Elements of the Science of Nutrition, Ed. 3, 1917, pp. 254 and 255.

the exception rather than the rule. The results have been so consistent in this regard that the conclusion seems justified that it may be considered to be of no very great value from the point of view of the addition of nitrogen to the body to increase the fat in a protein-fat diet.

Previous investigations, as summarized by Rosemann,[3] have yielded substantially the same results with alcohol on mixed diets as the present experiments do on protein-fat diets. The addition of alcohol did not spare nitrogen if given for a period of six days. It may be that if the observations had been continued, protein might have been saved to the body by utilization of alcohol, as was the case in Rosemann's observations. The alcohol, even more constantly than the fat, fails to bring about an assimilation of nitrogen, and is not to be recommended for the dietary of the diabetic if it is desired to spare protein.

The markedly positive nitrogen balances on the "carbohydrate-free diets" with high protein appear to solve the problem of what type of food is best suited to spare protein in the diabetic. The effort produced in these cases may be greater than that seen in normal individuals, inasmuch as most of these patients were either starved or kept on low diets for a considerable length of time before the systematic observations were begun. It has often been noted that it is exceedingly difficult to bring about "a prolonged deposition of protein in the normal adult, when fat is given with it."[4] In the diabetic, this apparently is not true for six-day periods, at least. Two experiments were conducted in which the high protein feeding was kept up for a longer period in order to illuminate this point. Case 10 (Table 2) was still retaining nitrogen at the rate of 6.7 gm. per day at the end of thirty-three days; Case 11 (Table 2) gave evidence of marked assimilation for twelve days, followed by twelve days in which the nitrogen balance shaded off to terminate in a nitrogen loss in the subsequent period. In summarizing these findings, it may be said that a positive nitrogen balance is readily achieved in diabetes on protein-fat diets with a high protein content, and that such an assimilation of nitrogen may persist for a considerable period before nitrogen equilibrium is reached.

It may be of interest to note in a few of these mild or moderately severe diabetics in whom the acid substances were determined in the urine (Table 2), that none of the food elements, when increased, whether protein, fat or alcohol, had any apparent effect on the amount of the acetone bodies excreted. This is somewhat at variance with the

3. Rosemann, R., in Oppenheimer's Handbuch der Biochemie des Menschen und der Tiere, 4, Part 1, p. 436.
4. Lusk, G.: Loc. cit., Footnote 2, p. 255.

well-known observations that especially the fats may be responsible for an increase of these substances and alcohol for their diminution. It is probable that the very severe diabetic reacts differently in this regard and that, over short periods at least, a high fat diet may result in no increase in the acidosis of moderately severe diabetics.

CONCLUSIONS

The addition of an equal number of calories of protein, fat or alcohol to a low caloric carbohydrate-free diet in cases of diabetes mellitus results in the assimilation of considerable amounts of nitrogen when the protein is used, a favorable nitrogen balance in only occasional instances with fat, and no change in the nitrogen equilibrium when alcohol is given. This would point to a high protein diet as the most advisable low-calory, carbohydrate-free diet by which to conserve the body tissues and furnish a maintenance ration for the diabetic.

CONTRIBUTIONS TO THE PHYSIOLOGY OF THE STOMACH

XLIX. HUNGER AND APPETITE IN PULMONARY TUBERCULOSIS *

JACOB MEYER, M.S., M.D.

Resident Physician, Cook County Hospital

CHICAGO

Recent studies by Carlson[1] and his co-workers emphasize the importance and the relative simplicity of an accurate study of hunger in normal and pathologic conditions. Cannon and Carlson have shown that the sensations of hunger are due to regular periodic contractions of the stomach. Deviations from the normal hunger sensations are associated with changes in the character of the hunger contractions and stomach tonus. This has been demonstrated in man and animals in many conditions such as gastric ulcer, gastric carcinoma, diabetes and gastritis. Meyer and Carlson[2] studied the condition of hunger and appetite in fever and found that the hunger contractions are absent in temporary fevers when the temperature reaches 103 F. and over, and that the dogs will not eat when febrile.

USUAL SYMPTOMS

Loss of appetite and absence of hunger are well recognized clinical manifestations of early and advanced pulmonary tuberculosis. The close relationship between the temperature of the patient and the gastric disturbances in tuberculous patients is well known. Thus, Klebs[3] asserts that a patient in advanced pulmonary tuberculosis who may have a good breakfast appetite will by midday and from that time on until the temperature falls again have no desire for food. Stockton[4] states that tuberculous patients with high temperatures have neither appetite or digestive ability. He also states that gastric dilatation and atony are common in tuberculosis. Conforming to this Klebs states that if the stomach is mapped out in advanced cases dilatation

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* From the Tuberculosis Hospital of Cook County Hospital.

1. Carlson, A. J.: Control of Hunger in Health and Disease, University of Chicago Press, 1917.

2. Meyer, J., and Carlson, A. J.: Contributions to the Physiology of the Stomach. XLII—Hunger and Appetite in Fever, Am. Jour. Physiol., 1917, **44**, 222.

3. Klebs, A. C.: Tuberculosis, New York, D. Appleton & Co., 1909.

4. Stockton, C. G.: Diseases of the Stomach, New York, D. Appleton & Co., 1914.

of the stomach will be found in a large percentage of cases and in some early cases. On the other hand, cases of tuberculosis with persistent temperature are readily relieved of this temperature elevation by correction of the gastric complaint.

THE PRESENT WORK

The present study was conducted on six patients with early, moderately advanced, and far advanced pulmonary tuberculosis. None of the patients showed signs of peritoneal or intestinal involvement or had any gastric complaint other than loss of appetite. These precautions were taken because it is well known that lesions of the peritoneum, intestine or stomach exert an inhibitory influence on gastric contractions.

The method pursued was briefly as follows: The patients were carefully examined after a clinical diagnosis of pulmonary tuberculosis was made, this being confirmed by routine sputum analysis and roentgen-ray examination. The temperature was recorded and the patient observed for a period of four to seven days before any work was commenced. In general, the cases selected were those showing a temperature of from 100 to 101 F. at some time during the day. On the day before the kymograph tracing was taken the patient was given his supper at 4 p. m. and nothing thereafter. The experiment was started at 8 a. m. the following morning, so that the starvation period was about sixteen hours. In order to obtain a record coincident with the afternoon rise in temperature a number of experiments were begun at 11 a. m. Patients have no difficulty in swallowing the balloon after one or two attempts. The great difficulty is to obtain from the patient an expression of his sensations with the hunger contractions. The patients in the Cook County Hospital are foreigners for the most part, and it is not only difficult to explain to them what is desired but even more difficult to obtain an intelligent response to questions.

REPORT OF CASES

CASE 1.—*History.*—Anton A., Greek laborer, aged 23, complained of cough, pain in the chest, chilly sensations, fever and loss of appetite. The details of the history are unimportant.

Examination.—The physical findings were dulness over the left apex, fine râles and bronchovesicular breathing, flatness beginning at the level of the eighth dorsal vertebra, with diminished vocal and breath sounds. Traube's space was absent. There were scattered râles in the right apex and a pleuritic friction rub on the right. The sputum contained tubercle bacilli. The roentgen-ray report by Dr. Turley was: "The left apex is blocked out; pleurisy with effusion; right costodiaphragmatic angle is also obliterated."

Temperature Record.—From the date of entrance, Feb. 12, 1918, until the first day of the experiment on February 19, the average morning temperature was 96.6 F. The afternoon temperature was 99.4.

Fig. 1 (Case 1).—Normal hunger contractions in an early case of pulmonary tuberculosis. Subnormal temperature. At *x* food was placed before the patient, but he was not allowed to eat.

Observation of February 19.—A record of the stomach contraction was taken, preceded by a fast of sixteen hours. The record was taken from 8 a. m. until 12 m. The temperature during this period was 99 F. Contractions began about one-half hour after swallowing the balloon. They were normal and regular. The patient did not experience the contractions as such. When asked whether he felt hunger he did not seem to understand. He was told to squeeze the finger of the observer whenever he experienced discomfort or hunger pang. He failed to do this, and the experiment was discontinued at noon. He readily ate the dinner which was then offered him.

Second Observation.—Three days later, with the patient's temperature at 99 F., another record was taken, beginning at 11 a. m., allowing a starvation period of nineteen hours. The latent period before the stomach assumed any tonus was approximately one hour. Regular hunger contractions then appeared. The patient was then asked whether he felt hungry, but could give no intelligible response. In the midst of a period of hunger contractions food was placed before him, but he was not allowed to eat it. Figure 1 shows the gradual inhibition of hunger contractions at the sight of food.

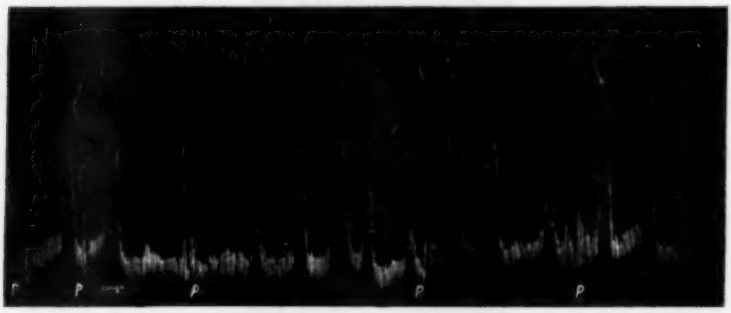

Fig. 2 (Case 2).—Vigorous contractions in an advanced case of pulmonary tuberculosis with marked cachexia, emaciation and septic temperature. Some of the contractions are incompletely recorded because they were so intense as to force the writing point out of the manometer.

Case 2.—*History.*—Anton K., Greek, aged 29, complained of having a cough for fifteen years. In the past two months he began to feel much weaker and complained of loss of appetite, loss of weight and night sweats.

Examination.—Physical findings were those of a cavity in the left upper lobe and complete involvement of the right lung. Fluoroscopic examination disclosed the presence of the cavity with a generalized pulmonary tuberculosis. The sputum contained numerous tubercle bacilli.

Temperature Record.—The temperature was characteristic of an advanced ulcerative type with subnormal temperature in the morning, rising to 102 and 103 F. in the afternoon.

Observation of February 25.—The usual period of fast was observed. The temperature of the patient during the observation ranged from 99.8 to 101 F. Hunger contractions began almost immediately after swallowing the balloon. They were vigorous, continued for an hour and were followed by a period of quiescence. The next period was characterized by more vigorous contractions than previously. With each contraction (Fig. 2) the patient became extremely restless, cried and pointed to his abdomen. When asked whether he was hungry or felt hunger, he cried and pointed to his epigastrium as if he were in pain. The patient died on March 4.

CASES 3 AND 4.—*History.*—These patients presented the same clinical picture as Case 2, and therefore the details of their findings are not here reported. The temperature records of these three patients were essentially alike, and death occurred in all three cases.

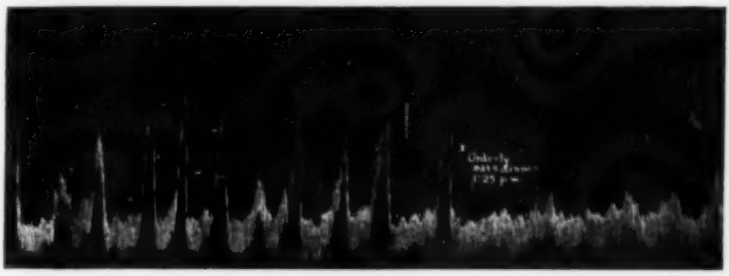

Fig. 3 (Case 3).—Vigorous contractions of another case of advanced pulmonary tuberculosis. At *x* the orderly ate his own meal in the presence of the patient. Compare also the effect in Figure 1.

Observation of March 11.—The temperature was 101 F. Contractions commenced immediately and were regular, periodic and extremely vigorous, lasting four hours. The patient could not say that he was hungry. At 1:30 p. m. the orderly of the ward brought his own meal into the room and ate it with the patient looking on. The hunger contractions almost immediately stopped (Fig. 3). Stomach tonus reappeared in fifteen minutes, followed again by vigorous contractions. At 2 p. m. a visiting physician entered the room, and again there was an immediate cessation of contractions.

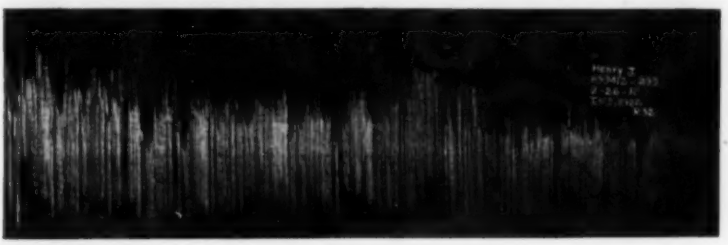

Fig. 4 (Case 4).—Entire absence of contractions in another advanced case. Temperature 102 F.

CASE 4.—*Observations of February 26.*—Temperature was 102 F. The usual period of fast was observed. After inflating the balloon in the stomach a few initial contractions occurred. These gradually disappeared, and for a period of one and three-quarter hours there were no contractions, nor any evidence of stomach tonus (Fig. 4). The patient vomited the balloon at the end of two hours, which necessitated repetition of inflation, and again contractions were present for a short time, followed by complete cessation. The temperature at the end of the period was 101.6. When asked if he desired food, he said he did not care. Food was placed before him, and he ate only a part of it.

Observation of February 27.—This revealed intense contractions so vigorous that the writing point was forced out of the manometer.

CASE 5.—*History.*—The patient, Harry W., presented a case of moderately advanced tuberculosis. He complained of cough, expectoration and shortness of breath. He volunteered that he would begin a meal thinking that he was hungry, eat a small part of it and leave it.

Examination.—The physical findings were those of dulness over the apex, bronchovesicular breathing and fine, scattered, crepitant râles bilaterally. The sputum was positive, and the roentgen ray revealed a generalized mottling with failure of the apices to light up.

Temperature Record.—This ranged from 97 to 101 and from 99 to 102 F.

Observation of February 21.—This began at 8 a. m. after a starvation period of sixteen hours. The stomach tonus was low, and the patient was very nervous. The temperature was 100 F.

Observation of March 1 after a starvation period of nineteen hours with temperature ranging from 99 to 101 during the tracing. At first there was a series of normal hunger contractions, followed by vigorous contractions felt as such and referred to the stomach. As the orderly ate his own dinner in full view of the patient, the contractions were only somewhat diminished to recur with still greater vigor (Fig. 5).

Fig. 5 (Case 5).—Normal contractions in a moderately advanced case with low-grade chronic temperature from 99 to 100.

CASE 6.—*History.*—The patient, Edward M., had a case of moderately advanced tuberculosis.

Observation.—This was taken with the temperature about 101 F. The contractions were only of moderate intensity, but nevertheless the patient stated that he felt something and said that he was hungry. At one point with no contractions he said he had an appetite and asked for whisky. This was promised, but not given. Stomach tonus continued, and one half hour later contractions appeared.

DISCUSSION OF RESULTS

The outstanding fact in all these observations is that contractions and stomach tonus are present. Case 1 presents an almost typical normal hunger contraction record. It is surprising to find in Cases 2, 3 and 4 such vigorous gastric contractions in view of the extreme cachexia, emaciation and advanced stage of the tuberculous process. Judging from the old clinical view, instead of an active stomach we

should expect dilatation and atony in advanced tuberculosis. The present observation in these patients of increased tonus and contractions accords with the observation of Luckhardt,[5] who noted increased hunger contractions in cases of cachexia associated with diabetic mellitus in man and in the cachexia of mangy dogs. The temperature of 101 F. apparently does not affect the hunger mechanism. In Case 4, however, with the temperature at 102 there is complete atony of the stomach and entire absence of the hunger contractions. This is also in accord with previous observations in animals. Cases 5 and 6 again point to the fact that patients with a low type of temperature persisting over a long period of time and with evident signs of intoxication present normal hunger contractions and stomach tonus.

COMMENT

The association in these cases of hunger contractions with absence of hunger sensations suggests the possibility that these contractions are probably not registered in consciousness as such. Again, in these cases the personal factor must be considered. Hunger contractions are present in some individuals, but instead of being recognized by the patient as such they are described as restlessness, headache and other symptoms. Again Carlson has recently shown that in long continued fasts hunger contractions are present, but are not recognized as such. This may be the case in chronic fevers, in which cases the hunger contractions are present.

5. Luckhardt, S.: Contributions to the Physiology of the Stomach—XI—The Cause of Polyphagia in Pancreatic Diabetes, Am. Jour. Physiol., 1914, **33**, p. 313.

THE ELECTROCARDIOGRAM IN THYROID DISEASE*

PAUL D. WHITE, M.D., AND JOSEPH C. AUB, M.D.
Lieutenants, M. C., U. S. Army

BOSTON

The effect of thyroid disease on the heart, and especially on the electrocardiogram, has been followed in the present investigation chiefly from two points of view. In twenty-three cases we have compared the severity of the disease, as shown by the variation of the total metabolism from the normal, with the amplitude of the T-wave in the electrocardiogram. In the second place, in forty-seven cases of hyperthyroidism we have determined the frequency and type of arrhythmia. Also heart rates, blood pressures and electrocardiographic evidence of left ventricular preponderance and of general muscular tremor have been of interest. The basal metabolism was determined by means of the Benedict Unit apparatus.[1] The electrocardiograms were taken with the Cambridge Model of the Einthoven string galvanometer and carefully standardized.

It has been said that the T-wave is high in hyperthyroidism and low, absent, or even inverted in hypothyroidism. In our series of cases there has been little if any parallelism between the basal metabolism and the amplitude of the T-wave in comparing different cases, but in individual cases, especially those with hypothyroidism with variations in the basal metabolism, there may occur corresponding changes in the height of the T-wave (see the accompanying table). In hypothyroidism the T-wave is low and increases under treatment. In hyperthyroidism it is also often low and its height does not parallel necessarily changes in the height of the metabolism; it sometimes runs conversely to it. In two of the patients suffering from auricular fibrillation while under treatment with digitalis, this drug had much more effect on the T-wave (flattening it) than had any differences of basal metabolism which these same patients showed.

Three of our forty-seven cases had paroxysms of auricular fibrillation, three had apparently permanent auricular fibrillation, one had paroxysms of auricular flutter with the normal rhythm interrupted by auricular premature contractions, while a number of others showed premature contractions.

* Submitted for publication June 22, 1918.
* From the Medical Clinic of the Massachusetts General Hospital.
1. Means, J. H., and Aub, J. C.: Jour. Am. Med Assn., 1917, **69**, 33.

TABLE SHOWING VARIATIONS IN T-WAVE

Case	Sex	Total Metabolism		Electrocardiograms		
		Date	Percentage Variation from the Normal	Date	T(10^{-4} Volts)	Pulse Rate
						A=auricular rate
C. A.	♀	11/13/16	+41	11/13/16	+2	A=120
(Case of complete heart-block. First seen while taking large doses of thyroid gland. This drug was stopped 11/16/16)		11/18/16	+40	11/18/16	+1	A=100
		11/20/16	+28	11/20/16	−1½	A=100
		12/ 4/16	+ 3	12/ 4/16	−1½	A= 75
		12/17/16	+14	12/23/16	+2	A= 78
		1/28/17	+ 8	1/31/17	+0	A= 95
M. T. P.	♀	11/ 7/16	+58	11/ 8/16	+1½	106
		2/28/17	+53	2/28/17	+2½	140
		4/18/17	+46	4/18/17	+1½	130
M. M.	♀	2/12/17	+74	2/ 7/17	+ ½	110
		3/27/17	+79	4/ 9/17	+2	108
				Partial thyroidectomy 4/16/17		
		4/29/17	+15	5/ 2/17	+3½	76
K. L.	♀	2/ 8/17	+26	2/ 7/17	+2	110
		4/28/17	+28	4/28/17	+2	110
V. D.	♀	2/15/17	+28	2/12/17	+4	120
		4/ 5/17	+27	4/ 5/17	+3	118
A. B.	♀	2/13/17	+37	2/ 8/17	+3	135
				Thyroidectomy right lobe and ⅓ left lobe 2/14/17		
		3/28/17	+ 4	3/28/17	+1½	110
M. H.	♀	2/17/17	+47	2/19/17	+1½	90
		3/ 7/17	+27	3/ 8/17	+3	100
B. M. T.	♀	3/12/17	+29	3/13/17	+5	150
		4/29/17	+47	4/16/17	+4	124
M. T.	♀	3/13/17	+64	3/13/17	+3	130
				Thyroidectomy right lobe and isthmus 3/27/17		
		4/ 1/17	+35	4/ 2/17	+2½	105
E. M.	♀	11/19/16	+24	11/16/16	0	120
		4/ 9/17	+ 1	4/ 9/17	− ½	105
E. S.	♀	10/ 7/15	+73	10/ 5/15	+4	100
		3/28/17	+87	3/28/17	+4½	130
C. M.	♀	3/29/17	+84	3/26/17	+3	130
		4/ 6/17	+67	4/ 9/17	+1½	107
J. B.	♀	2/17/17	+37	2/19/17	+3	75
T. W.	♀	4/17/15	+49	4/10/15	+2	85
A. L.	♀	5/ 2/17	+68	5/ 2/17	+2	110
C. J.	♂	4/ 3/17	+43	4/ 3/17	+3	110
P. B. K.	♀	4/10/17	+99	4/11/17	+2	124
E. H.	♀	6/ 5/17	+44	6/ 5/17	+3	80
T. D.	♂	3/12/17	+29	3/ 9/17	+1½	135
C. M.	♀	12/20/16	+74	12/20/16	0	160 (auricular fibrillation)
(Paroxysmal auricular fibrillation)		1/ 9/17	+34	1/10/17	−4 (digitalis effect)	108 (normal rhythm)
		2/ 1/17	+58	2/ 7/17	+2	122 (normal rhythm)
		4/24/17	+73	4/24/17	+3	130 (normal rhythm)

TABLE SHOWING VARIATIONS IN T-WAVE—(*Continued*)

Case	Sex	Total Metabolism		Electrocardiograms		
		Date	Percentage Variation from the Normal	Date	T(10^{-4} Volts)	Pulse Rate
E. T. B. (Paroxysmal auricular fibrillation)	♂	2/ 3/17	+71	2/ 5/17	−2	115 (normal rhythm)
		2/16/17	+61	2/13/17	−2	145 (auricular fibrillation)
		2/25/17	+69	2/23/17	−6 (digitalis effect)	108 (auricular fibrillation)
		(Thyroidectomy, right lobe and isthmus, 3/5/17)				
		3/14/17	+34	3/13/17	−4½	90 (normal rhythm)
		4/ 7/17	+67	4/ 7/17	−1	126 (normal rhythm)
E. R.	♀	11/14/14	−25	11/12/14	0	82
		11/23/14	−15	11/23/14	1½	87
		(After 24 grains of thyroid gland extract in 8 days)				
H. L. (Under treatment for cretinism)	♀	2/14/17	−17	2/14/17	−2½	98
		3/ 7/17	+ 5	3/ 7/17	0	105
		3/16/17	+ 1	3/14/17	+1	112
		4/24/17	+20	4/24/17	+2	120

The degree of tachycardia paralleled the basal metabolism percentage but moderately. In one unusual case of complete heart block (C. A. in the table) the ventricular rate showed but a few beats change between the time of hyperthyroidism and the time of normal basal metabolism. In this case, however, as reported in a previous paper,[2] the auricular rate as shown electrocardiographically varied with the basal metabolism; 120 per minute at + 42.5 per cent. and 75 per minute at + 3 per cent.

Left ventricular preponderance was found by the electrocardiogram in only three of twenty-seven of hyperthyroidism. The index of preponderance in these cases was from + 26 to + 30. The normal borderline of this index is from + 20 to + 30 as described in a previous paper.[3] Variable hypertension was frequently present with figures of 150 to 200 mm. mercury systolic and 90 to 110 mm. diastolic. In one case the pressure dropped within a few weeks from 210 mm. to 130 mm. systolic and from 100 mm. to 75 mm. diastolic, while the basal metabolism decreased from + 47 per cent. to + 27 per cent.; in this case the T-wave rose in amplitude from 0.15 to 0.28 millivolt. General muscular tremors shown electrocardiographically are common in hyperthyroidism.

2. Aub, J. C., and Stern, N. S.: THE ARCHIVES INT. MED., 1918, **21,** 130.
3. White, P. D., and Bock, Am. Jour. Med. Sc., 1918, **156,** 17.

SUMMARY

Very limited parallelism has been found between the basal metabolism and the amplitude of the electrocardiographic T-wave in a series of twenty-seven cases of thyroid disease.

Auricular fibrillation, including the paroxysmal type, is not uncommon in hyperthyroidism as shown in our series by six out of forty-seven cases of hyperthyroidism (13 per cent.). Paroxysmal auricular flutter has been seen in one of our cases.

Tachycardia, frequent hypertension and frequent tremor while at rest occurred in the cases of hyperthyroidism although not always parallel to the total metabolism.

RENAL FUNCTION AS MEASURED BY THE ELIMINATION OF FLUIDS, SALT AND NITROGEN, AND THE SPECIFIC GRAVITY OF THE URINE

II. THE EFFECT OF HIGH, LOW AND NORMAL DIETS *

HERMAN O. MOSENTHAL, M.D. (NEW YORK)
BASE HOSPITAL, CAMP GORDON, ATLANTA, GA.

Since Hedinger and Schlayer[1] introduced the method of testing renal function by measuring the volume and the specific gravity and estimating the sodium chlorid output in two-hourly specimens of urine throughout the day and in a single specimen during the night, it has received general acceptance in this country. In conducting the test, much stress was laid on the fact that the diet necessary to produce satisfactory results must contain a considerable quantity of the diuretic substances ordinarily found in the food, such as fluids, salts and purins. Two forms of diets have been used fairly extensively, the one consisting of three meals,[2] the other of five.[3] The results obtained in both appear to be very similar. In order to obtain a clear understanding of this method of testing renal function, it was necessary to formulate precisely what the normal reaction was. This was attempted.[4] Since that report was made, a large number of normal tests have been carried out, and in the light of these it becomes apparent that the former standards are wrong in some respects and should be corrected. The question as to what diet should be used in carrying out this test is a far-reaching one. If the diet need not be limited in any way, there is a wider field of usefulness for the test, especially in general practice. In the present paper, the attempt will be made to define as closely as possible the normal results of this method of analyzing the urine on various diets and to note the value of widely divergent diets in cases with impaired renal function.

FORMS OF DIETS

The diets employed were three: a high protein diet; a low protein diet, and a normal diet. The *high protein diet* was the one originally advocated for the performance of the test.[2] It contains about the amount of protein that a normal individual with a good appetite will consume. The designation "high protein diet" may, therefore, be a misnomer. However, it is so designated to indicate the contrast with

* Submitted for publication May 23, 1918.
* From the Medical Clinic of The Johns Hopkins Hospital.

1. Hedinger and Schlayer: Deutsch. Arch. f. klin. Med., 1914, **114,** 120.
2. Mosenthal, H. O.: THE ARCHIVES INT. MED., 1915, **16,** 733.
3. O'Hare, J. P.: THE ARCHIVES INT. MED., 1916, **17,** 711.
4. Mosenthal, H. O., and Lewis, D. S.: Jour. Am. Med. Assn., 1916, **67,** 933.

the other diets. This diet contains approximately 1,760 c.c. of fluid, 8.5 gm. of salt and 13.4 gm. of nitrogen, and considerable quantities of purin substances in the soup, meat, tea and coffee. The *low protein diet* was that in use at this hospital.* It was found that when no restrictions were placed on the persons taking this diet, protein equivalent to from 3 to 4 gm. of nitrogen was usually consumed in the twenty-four hours. This was deemed sufficiently low for the purposes of the present observations. The diet contained no tea or coffee or purins in any form. Some alcohol was allowed as sherry. This was given in less than one-half of the cases studied. The remainder of the food consisted largely of starches, which have a marked effect in preserving the body protein and thereby limiting the amount of waste products to be excreted in the urine. The *normal diet* consisted of the food which the subject chose. The aim was to determine whether it was possible to allow a person to continue his normal dietary habits while the test was carried out. In the remainder of this article these diets will be spoken of respectively as the high, the low, or the normal diet.

The only other restrictions placed on the persons tested were that no food or fluid should be taken between meals, and that the collection of the night specimens should begin three hours after supper. The specimens were usually collected at two-hourly intervals from 8 a. m. to 8 p. m. If supper were taken after 5 p. m., the collection of the night specimen was begun at a correspondingly later time. It may be that it is not necessary to limit the frequency with which fluid and food are taken; however, it did not seem advisable to attempt too much at one time, and it was deemed best not to extend the variations too much so that clear-cut results might be obtained.

The specific gravity of the urine was measured at room temperature by reliable floats; the nitrogen was determined by the Kjeldahl process and the sodium chlorid by the method of Volhardt. The normal persons tested were men and women of the teaching staff and student body.

THE NORMAL STANDARD

The normal standard as advocated previously was as follows: A maximum specific gravity of 1.018 or higher, a variation of 9 degrees or more between the minimum and maximum specific gravity readings, and a night urine of 400 c.c. or less, with a specific gravity of 1.018 or over and a concentration of nitrogen of at least 1 per cent. (Table 1).

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* *Breakfast:* Sherry (30 c.c.), baked apple, stewed prunes, orange, hominy cornstarch (⅔ hominy, ⅓ cornstarch), cereal, cream (15 c.c.), sugar, butter.
Dinner: Sherry (30 c.c.), potato, baked or mashed, string-beans, cabbage, carrots, lettuse, onions, tomatoes, cucumber pickles, fruit cornstarch pudding, fruit tapioca pudding, sugar, butter.
Supper: As dinner.

At the time these criteria were formulated, it was not realized how profoundly the activity of the kidney may be affected by many influences. Nervous tension, very hot or cold weather, and what may be termed the "renal habits" of any person, all have appeared to play a distinct rôle in causing differences to appear that were not at first appreciated. Lyle and Sharlit[5] have called attention to the fact that the night urines in normal persons may exceed 400 c.c. by a considerable margin and that the variations in the specific gravity may be less than 9 and that there are instances in which the concentration of nitrogen in the night urine is less than 1 per cent. The results of Lyle and Sharlit in regard to the fixation of the specific gravity are probably somewhat exaggerated as they obtained them when the subjects were kept for several days on a diet constant in fluids as well as solids. This introduces a new factor for which due allowance must be made. The same phenomenon may be noted in the observations to be recorded in this communication, but not to the same degree. The presence of larger amounts than 400 c.c. in the night urine and a concentration of nitrogen of less than 1 per cent. in the night urine has been a rather common finding in the present series of normals.

TABLE 1.—Results of a Test Meal for Renal Function in a Normal Person. This Table Shows at What Intervals the Urine Was Collected. It Meets All the Requirements which Were Formerly Regarded as Characteristic of a Normal Test.

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen	
			Per Cent.	Grams	Per Cent.	Grams
8-10	315	1.006				
10-12	128	1.014				
12- 2	120	1.017				
2- 4	122	1.020				
4- 6	76	1.022				
6- 8	100	1.027				
Total, Day	861	....	0.78	6.71	0.79	6.80
Night, 8-8	248	1.025	0.69	1.71	1.23	3.05
Total, 24 Hours	1,109	....	....	8.42	....	9.85
Intake	1,760	....	....	8.50	....	13.40
Balance	+651	....	....	+0.08	....	+3.55

Table 1 may serve to recall what determinations are carried out and how a test meal for renal function is recorded. In the interpretation of this procedure as a means of measuring renal activity, certain points, the maximum specific gravity, the variation in specific gravity, the quantity of the night urine and its specific gravity and concentra-

5. Lyle, W. G. ,and Sharlit, H.: The Archives Int. Med., 1918, **21**, 366.

tion of nitrogen have been emphasized. There are probably other features that deserve to be considered in this connection; however, thus far there are no observations that have laid any stress on them. In Tables 2, 3, 4 and 5, in order to save space, only a summary of what

TABLE 2.—SUMMARY OF RESULTS OF THE COLLECTION OF URINARY SPECIMENS AT TWO-HOURLY INTERVALS DURING THE DAY AND FOR A TWELVE-HOUR PERIOD AT NIGHT IN NORMAL PERSONS WHILE ON THE "HIGH" DIET.

Date	Day of Diet	Specific Gravity*				Night Urine	
		Highest	Lowest	Degrees Variation	Night Urine	Nitrogen, Per Cent.	Volume, C.C.
6/27/17	1	34	30	4	34	2.70	160
6/11/15	1	33	24	9	29	1.85	218
5/ 9/17	2	33	05	28	31	1.63	175
6/19/17	1	30	05	25	25	1.19	294
6/27/17	1	29	13	16	29	....	....
11/21/17	1	29	07	22	22	....	258
5/19/17	2	28	07	21	14	0.61	826
5/18/17	1	28	03	25	21	1.25	170
2/10/14	3	28	08	20	23	1.30	374
11/22/17	2	27	06	19	15	....	425
5/18/17	1	27	03	24	26	1.48	169
6/10/15	1	27	06	21	25	1.22	248
11/22/17	2	27	08	19	18	....	456
11/22/17	2	27	09	18	19	1.28	334
6/19/17	1	25	15	10	15	0.87	506
2/14/16	2	25	07	18	25	1.58	240
1/17/16	1	24	09	15	23	1.43	350
5/18/17	1	22	05	17	08	0.56	417
5/19/17	2	22	06	16	09	0.54	539
1/17/16	1	21	08	13	21	1.19	350
2/14/16	1	21	07	14	19	0.95	400
12/11/14	3	20	10	10	20	1.22	375
12/12/14	1	20	07	13	18	0.76	568
2/10/17	3	20	09	11	13	0.74	615
6/ 3/15	1	19	07	12	19	1.14	356
4/15/15	1	19	07	12	17	1.20	332
11/21/17	1	19	07	12	19	....	280
4/ 6/15	1	19	09	10	19	1.12	350
2/10/17	1	19	06	13	13	0.62	721
12/ 5/14	2	18	08	10	15	1.08	402
6/ 3/15	1	18	06	10	18	1.08	290
11/ 2/17	1	14	08	6	13	....	660

* Last two figures only.

may be considered the salient features of test meals for renal function, as carried out in normal subjects, while on high, low or normal diets, is given.

TABLE 3.—Summary of the Results of the Collection of Urinary Specimens at Two-Hourly Intervals During the Day and for a Twelve-Hour Period at Night in Normal Persons while on the "Low" Diet.

Date	Day of Diet	Specific Gravity*				Night Urine	
		Highest	Lowest	Degrees Variation	Night Urine	Nitrogen, Per Cent.	Volume, C.C.
11/23/17	1	36	12	24	12	0.47	565
6/28/17	1	34	13	21	20	1.44	260
11/23/17	2	30	13	17	13	....	525
11/23/17	1	30	07	23	18	....	104
6/16/17	2	30	07	23	12	0.45	475
1/20/16	3	29	06	23	29	1.14	215
6/29/17	2	29	05	24	19	1.26	197
11/24/17	2	28	12	16	12	....	408
2/15/16	1	28	16	12	27	0.50	210
6/16/17	2	28	05	23	11	0.62	391
1/20/16	3	27	12	15	27	1.57	178
2/15/16	1	27	10	17	25	1.41	267
11/23/17	1	26	06	20	20	....	174
11/24/17	2	26	09	17	13	....	554
1/18/16	1	26	06	20	26	1.24	195
6/29/17	2	25	03	22	25	1.41	188
1/19/16	2	25	06	19	25	1.29	210
6/28/17	1	25	05	20	20	0.95	340
2/ 7/17	3	25	06	19	15	0.74	429
6/21/17	2	25	05	20	13	0.84	315
2/ 7/17	1	25	10	15	25	1.30	210
2/16/16	2	24	09	15	24	0.83	240
6/20/17	1	24	11	13	19	1.38	167
5/16/17	1	24	02	22	15	0.87	280
2/17/16	3	23	14	9	23	0.66	300
2/ 7/17	3	23	07	16	13	0.23	523
1/19/16	2	23	07	16	23	....	230
1/18/16	1	22	06	16	22	1.23	220
5/16/17	1	22	03	19	11	0.52	489
5/17/17	2	21	03	18	09	0.31	637
2/16/16	2	21	06	15	21	0.74	300
2/17/16	3	21	12	9	20	0.69	255
5/16/17	1	20	03	17	09	0.46	512

* Last two figures only.

TABLE 4.—Summary of Results of the Collection of Urinary Specimens at Two-Hourly Intervals During the Day, and for a Twelve-Hour Period at Night in Normal Persons while on Their Customary "Normal" Diets.

Date	Specific Gravity*				Night Urine	
	Highest	Lowest	Degrees Variation	Night Urine	Nitrogen, Per Cent.	Volume, C.C.
6/18/17	37	20	17	26	1.73	331
11/20/17	36	16	20	16	....	660
7/ 9/16	33	25	8	31	....	100
10/23/16	33	15	18	15	....	568
10/24/16	32	18	14	25	....	370
7/ 8/16	31	23	8	31	....	210
6/11/16	31	14	17	30	2.05	340
10/18/16	31	20	11	31	....	94
6/26/17	31	16	15	27	1.84	224
6/26/17	30	25	5	30	....	275
5/15/17	30	09	21	22	1.40	369
5/ 9/16	30	19	11	20	1.31	350
10/29/14	30	26	4	27	2.07	290
3/18/16	30	21	9	30	2.26	240
3/23/16	30	10	20	30	1.63	250
7/11/16	30	09	21	29	....	185
7/21/16	30	18	12	25	....	186
10/23/16	30	26	4	26	....	260
10/18/16	30	13	17	16	....	750
5/15/16	30	12	18	12	0.85	440
10/23/16	30	24	6	24	....	500
11/20/17	30	07	23	28	1.32	266
6/21/17	29	18	11	24	....	373
7/20/16	29	19	10	25	....	196
7/10/16	29	22	7	24	....	235
11/20/16	29	14	15	20	....	645
10/25/16	29	19	10	22	....	422
7/12/16	28	22	6	28	....	198
10/20/16	28	21	7	28	....	270
10/25/16	28	20	8	28	....	268
10/19/16	28	10	18	28	....	300
10/19/16	28	12	16	28	....	226
11/19/17	28	08	20	17	....	398
7/17/16	27	20	7	27	....	222
6/10/16	27	16	11	27	1.61	330

TABLE 4.—(*Continued*)

Date	Specific Gravity*				Night Urine	
	Highest	Lowest	Degrees Variation	Night Urine	Nitrogen, Per Cent.	Volume, C.C.
7/10/16	26	12	14	23	....	105
7/16/16	26	13	13	26	....	210
11/19/16	26	10	16	26	....	395
6/10/16	26	14	12	21	....	330
10/18/16	26	13	13	20	....	320
10/26/16	26	10	16	21	....	305
11/19/16	26	12	14	21	....	250
5/14/17	25	12	13	15	0.87	467
6/20/17	25	17	8	19	....	430
7/22/16	25	10	15	25	....	170
7/ 9/16	25	04	21	17	....	255
6/ 9/16	25	13	12	17	1.08	735
10/19/16	25	09	16	15	....	506
10/25/16	25	18	7	22	....	525
10/18/16	25	15	10	19	....	312
10/18/16	25	08	17	21	....	375
10/24/16	25	13	12	24	....	530
10/26/16	25	19	6	25	....	510
10/30/17	25	05	20	18	1.43	861
10/19/16	24	22	2	22	....	506
5/15/17	23	08	20	14	0.85	443
3/23/17	23	07	16	22	1.46	475
7/15/16	23	03	20	15	....	180
10/19/16	23	09	14	16	....	305

* Last two figures only.

TABLE 5.—Summary of Salient Facts on the Urinary Specimens Collected During Periods of "High," "Low" and "Normal" Diets in Normal Persons.

	Number of Observations		
	"High" Diet	"Low" Diet	"Normal" Diet
Maximal specific gravity:			
30 or higher	4	5	22
29 to 25	12	16	32
24 to 20	8	12	5
19 or 18	7	0	0
Less than 18	1	0	0
Total number of observations	32	33	59
Degrees of variation of specific gravity:			
13 or over	20	26	32
12 to 9	10	7	12
8 to 5	1	0	12
4 or less	1	0	3
Total number of observations	32	33	59
Specific gravity of night urine:			
21 or over	13	13	41
20 to 18	10	7	6
17 to 15	3	2	10
14 to 10	4	9	2
Less than 10	2	2	0
Total number of observations	32	33	59
Volume c.c. of night urine:			
400 or less	21	23	42
401 to 500	4	4	7
501 to 600	3	5	6
601 to 700	2	1	2
701 to 750	1	0	2
Total number of observations	31	33	59
Nitrogen per cent. in night urine:			
1% or higher	18	11	13
0.99% to 0.80%	2	5	3
0.79% or less	6	11	0
Total number of observations	26	27	16

In Tables 2, 3 and 4 the results of the tests for renal function are given for the high, low and normal diets. They are arranged in order from those with the highest maximum specific gravity to those with the lowest. The dates on which the tests were made are included because they indicate that all seasonal variations, especially as far as temperature is concerned, are taken into consideration. The number of days on which an individual was on a given diet are recorded, as this may naturally have some bearing on the result.

THE MAXIMAL SPECIFIC GRAVITY IN NORMAL TESTS

The last test noted in Table 2 on the high diet is remarkable. It is the only example in the tests (including those of Tables 3 and 4 on the low and normal diets) in which the maximum specific gravity was lower than 1.018. This may be a faulty observation, or it may be a phenomenon of rare occurrence. This person's other test meals, five in number, all yielded specific gravities comparable with other normals, and her phenolsulphonephthalein excretion, blood urea and total non-protein nitrogen and Ambard's constant were strictly within normal limits. Taking all the tests (124 in number, Table 5) into consideration, it is apparent that such a low maximum specific gravity is likely to be found in less than 1 per cent. of normal persons, and may be disregarded. It is probably due to some anomalous water excretion, which occurs very rarely.

In the other tests it was found that the maximum specific gravity was always 1.018 or higher on the high diet, and 1.020 or over on the low or normal diets. Evidently, this is one of the most constant features to be relied on in estimating normal renal function by the test meal procedure. This may possibly be more forcibly demonstrated in Chart 1. Here it may be noted how in general the quantity of salt and nitrogen excreted varied according to the diet, and yet the fluctuations in the specific gravity reached a maximum of at least 1.018 on the high diet and 1.020 on the low or normal diets on each day.

In order to obtain a more complete knowledge of the reasons for a certain maximal concentration in the various specimens of this method of collecting urines, as well as for the other phenomena to be taken up in detail subsequently, it was decided to give a diet whose influence on the kidney should be as nearly uniform as possible. This was accomplished by means of starvation. A constant quantity of water was given at two-hourly intervals, at the time when the period for each day specimen was begun. This was successfully carried out in five experiments; in two others, the water was taken in varying amounts and in one the quantity of water drunk was not noted. The

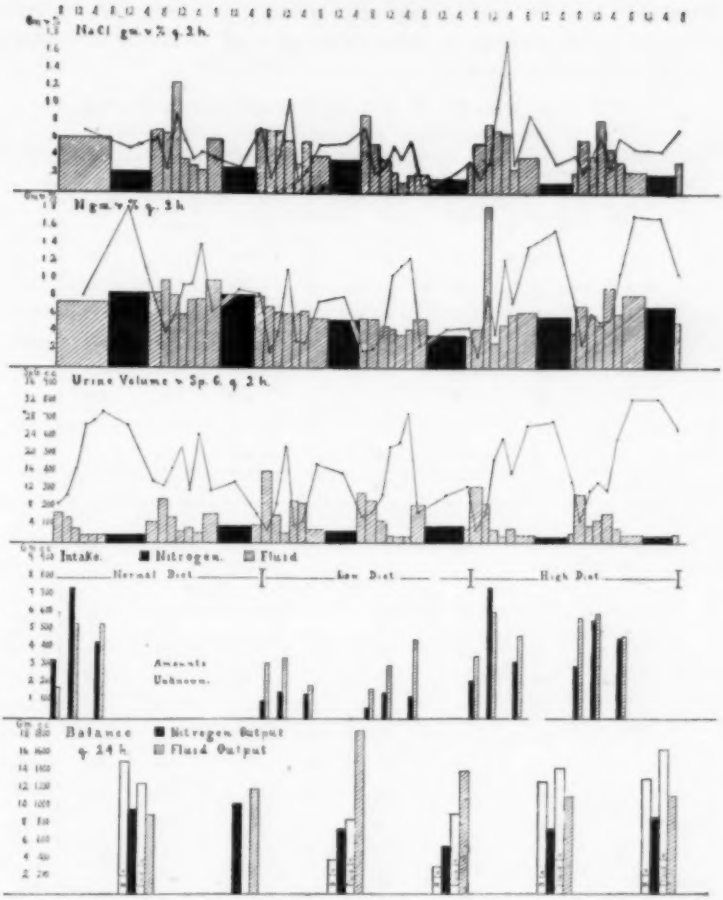


Chart 1.—Results of frequent collections of urine in the day time and a single specimen of urine at night in a normal individual for a period of six days. It shows how the variations of volume of urine, specific gravity and concentration of NaCl and N are somewhat similar whether the diet is normal, low or high.

Explanation of the Chart: The height of the columns in the spaces for NaCl, N and urine volume indicate the two-hourly rate of excretion (they are not absolute values as in the remaining charts); the width of each column represents the period of time covered by the individual specimen; the night urines are indicated in the solid black, the day specimens in oblique hatching. The dots joined by continuous lines crossing the upper three tiers from left to right indicate the percentage concentrations of NaCl and N and the specific gravity, respectively. In the second tier the columns represent absolute values for N and fluid taken at each meal. The dividing line between the solid black (N) and cross hatched (fluid) column indicates the time at which the meal was taken. The columns in the first tier record the fluid and N balance for the preceding twenty-four hours.

results, because of their great interest and importance for the more thorough understanding of the normal mode of action of the kidney, are given in full in Table 6.

TABLE 6.—Results in Normal Persons while Fasting

Observation 1. First Day of Starvation.

Water Intake		Urine						
Time	C.C.	Time	C.C.	Sp. Gr.*	NaCl		N	
					%	Gm.	%	Gm.
8	200	8-10	245	11	0.64	1.57	0.49	1.20
10	200	10-12	345	08	0.52	1.79	0.31	1.07
12	200	12- 2	92	15	0.82	0.75	0.89	0.82
2	200	2- 4	92	18	0.52	0.48	0.92	0.85
4	200	4- 6	390	07	0.16	0.62	0.26	1.01
6	200	6- 8	122	17	0.50	0.66	0.80	1.17
Total, day.....	1,200		1,296			5.87		6.12
Night.....	0	8- 8	205	27	0.74	2.18	1.69	4.99
Total, 24 hours..	1,200		1,501			8.05		11.11

Observation 2. First Day of Starvation.

Water Intake		Urine						
Time	C.C.	Time	C.C.	Sp. Gr.*	NaCl		N	
					%	Gm.	%	Gm.
8	250	8-10	100	17	1.02	1.02	0.76	0.76
10	250	10-12	45	22	0.78	0.35	1.13	0.51
12	250	12- 2	56	22	0.90	0.53	1.16	0.65
2	250	2- 4	268	05	0.18	0.48	0.30	0.80
4	250	4- 6	202	08	0.16	0.32	0.40	0.81
6	250	6- 8	174	08	0.16	0.28	0.38	0.66
Total, day.....	1,500		845			2.98		4.19
Night..... 8	250	8- 8	900	10	0.16	1.44	0.49	4.41
Total, 24 hours..	1,750		1,745			4.42		8.60

Observation 3. First Day of Starvation.

Water Intake		Urine						
Time	C.C.	Time	C.C.	Sp. Gr.*	NaCl		N	
					%	Gm.	%	Gm.
8	250	8-10	40	27	0.66	0.26	1.37	0.55
10	250	10-12	325	04	0.38	1.24	0.25	0.81
12	250	12- 2	450	04	0.34	1.53	0.16	0.72
2	250	2- 4	265	06	0.22	0.60	0.30	0.62
4	250	4- 6	178	05	0.24	0.43	0.29	0.52
6	250	6- 8	204	05	0.22	0.45	0.22	0.45
Total, day.....	1,500		1,462			4.57		3.67
Night.....	0		257	20	0.42	1.08	0.94	2.42
Total, 24 hours..	1,500		1,650			5.65		6.09

TABLE 6.—Results in Normal Persons while Fasting—*Continued*

Observation 4. Second Day of Starvation.

Water Intake		Urine						
Time	C.C.	Time	C.C.	Sp. Gr.*	NaCl		N	
					%	Gm.	%	Gm.
8	250	8-10	70	21	0.24	0.17	0.95	0.67
10	250	10-12	110	18	0.26	0.29	0.78	0.86
12	250	12- 2	158	14	0.22	0.35	0.58	0.92
2	250	2- 4	440	05	0.10	0.44	0.22	0.97
4	250	4- 6	295	09	0.14	0.41	0.27	0.80
6	250	6- 8	234	08	0.22	0.51	0.32	0.75
Total, day.....	1,500		1,307			2.17		4.97
Night.....	0	8- 8	770	15	0.20	1.54	0.56	4.31
Total, 24 hours..	1,500		2,077			3.71		9.28

Observation 5. First Day of Starvation.

Water Intake		Urine						
Time	C.C.	Time	C.C.	Sp. Gr.*	Na_2Cl		N	
					%	Gm.	%	Gm.
8	150	8-10	50	20	0.95	0.48	1.01	0.51
10	150	10-12	104	17	1.14	1.19	0.78	0.81
12	150	12- 2	77	17	1.15	0.89	0.85	0.65
2	150	2- 4	115	13	0.72	0.83	0.73	0.84
4	150	4- 6	65	20	0.84	0.55	1.03	0.67
6	150	6- 8	96	15	0.52	0.50	0.77	0.74
Total, day.....	900		507			4.44		4.22
Night.....	0	8- 8	308		0.54	1.66	1.58	4.87
Total, 24 hours..	900		815			6.10		9.09

Observation 6. First Day of Starvation.

Water Intake		Urine						
Time	C.C.	Time	C.C.	Sp. Gr.*	NaCl		N	
					%	Gm.	%	Gm.
8	250	8-10	96	25	1.78	1.69	0.73	1.69
10	250	10-12	405	06	0.26	1.05	0.15	0.61
12	175	12- 2	300	06	0.36	1.08	0.22	0.66
2	175	2- 4	340	08	0.22	0.75	0.15	0.52
4	175	4- 6	135	10	0.60	0.81	0.36	0.49
6	175	6- 8	34	16	0.94	0.32	0.60	0.20
Total, day.....	1,400		1,309			6.60		4.17
Night.....	0	8- 8	150	23	0.82	1.23	0.98	1.40
Total, 24 hours..	1,400		1,459			7.83		5.57

TABLE 6.—Results in Normal Persons while Fasting—*Continued*

Observation 7. Second Day of Starvation

	Water Intake		Urine		
	Time	C.C.	Time	C.C.	Sp. Gr.*
	8	175	8-10	34	27
	10	175	10-12	102	12
	12	350	12- 2	122	10
	2	350	2- 4	385	05
	4	175	4- 6	375	05
	6	0	6- 8	202	07
Total, day		1,225		1,220	
Night		0	8- 8	460	22
Total, 24 hours		1,225		1,680	

Observation 8. Second Day of Starvation

	Water Intake		Urine		
	Time	C.C.	Time	C.C.	Sp. Gr.*
			8-10	77	24
			10-12	45	25
		Not Noted	12- 2	64	25
			2- 4	44	26
			4- 6	60	25
			6- 8	63	26
Total, day		?		353	
Night		?	8- 8	475	17
Total, 24 hours		?		828	

* Last two figures only.

It is evident that even in starvation there is a maximum concentration of 1.020 or over. This would not have been the case had water been forced continuously, as has been done by a number of observers. Under such conditions there is a continuous flow of urine of low specific gravity. In the present studies only such amounts of water as the person was supposed to desire were taken at regular intervals, thus providing a constant stimulus to diuresis. Under such circumstances there appear to be two types of response, one seen in Observation 8 (Table 6), the other in the remaining experiments. In Observation 8 there was no record of the water intake; presumably, however, it was low, as the specific gravity remained high and fairly constant throughout the day; Observation 5, with a comparatively low water intake (150 c.c. every two hours) approximates this result. In the other observations, when the water intake was higher, there was at least one specimen in the twenty-four hours that reached 1.021 or higher. This is in large part due to the fact that in spite of the constant water intake,

there was at intervals a large urine output, exceeding the intake by a considerable margin, followed by a period of comparative oliguria. It seemed as though, if the resistance which the diuretic stimulus encountered were once overcome, the kidney continued to act and drain the body of as much fluid as was available, acting much on the principle of a syphon. Thus, there would be either one (Observations 2, 3, 4, 6 and 7, Table 6, and Observation 4, Chart 2) or two periods of diuresis (Observation 1, Table 6, and Chart 2) during the day.

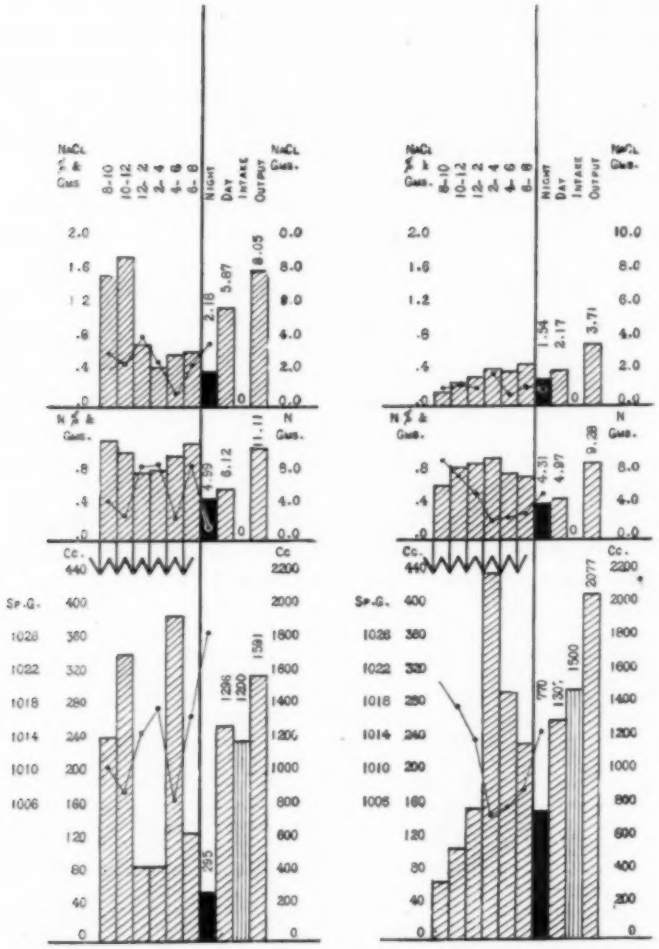
That the specific gravity varies in inverse proportion to the quantity of fluid excreted is readily appreciated. It is this factor of variability in the water output, in spite of a constant fluid intake, that evidently is, in part at least, responsible for the production of a specific gravity of 1.020 or over during some period of the day or night in normal persons. The quantity of nitrogen excreted remains fairly constant from period to period, being at times slightly higher when diuresis occurs. The sodium chlorid has a tendency to be much higher in the morning hours than in the afternoon on the first day of starvation. Here again during the period of high urine output the salt excretion is frequently, though not always, raised. These facts are brought out clearly in Chart 2. The one observation (Observation 4, Table 6 and Chart 2) covering the second day of starvation indicates that the sodium chlorid output becomes constant from hour to hour at that time.

Explanation of the Charts.—Except Charts 1 and 4, each chart is divided by two horizontal lines into three tiers. The lowest of these gives the figures for water and specific gravity, the middle for nitrogen and the upper for sodium chlorid. Each is further divided by a central vertical line into right and left halves. The left half, with its scale at the extreme left, contains six columns for the two-hourly specimens collected between 8 a. m. and 8 p. m. Each column represents absolute values. The right half is read by the scale at the extreme right. The columns of this right half are two pairs; the central pair represents the total night and the total day twelve-hour figures for volume, nitrogen and sodium chlorid, night in solid black and day in oblique hatching at its right. The pair at the extreme right represent intake and output for the whole twenty-four hours, intake at the left in vertical, output at the right in cross or oblique hatching. The dots joined by continuous lines crossing each tier from left to right indicate the specific gravity and the percentage concentrations of nitrogen and sodium chlorid, respectively, and are read from the scale at the left.

It seems justifiable to conclude, therefore, that a normal individual will void at least one specimen a day, when the urine is collected according to the method under discussion, of a specific gravity of 1.018 or more on any diet, and of 1.020 or higher on the low or normal diets.

THE VARIATION OF SPECIFIC GRAVITY IN NORMAL TESTS

From Tables 2, 3, 4 and 5 it is evident that in normal individuals there is usually a variation of specific gravity of 9 points or more while on the high and low diets, but that the variation may be much less on



First Day of Starvation

↓ Indicates the time at which 200 c.c. of fluid were taken (corresponds to Observation 1, Table 6).

Second Day of Starvation

↓ Indicates the time at which 250 c.c. of fluid were taken (corresponds to Observation 4, Table 6).

Chart 2.—Results of two-hourly collections of urine in the day time and a single specimen at night in normal individuals, while taking no food or fluid except water. Note the marked variations in the volume and specific gravity, and the concentrations of N and NaCl in the urine, in spite of the constant fluid intake.

the normal diet. It would seem that this is largely a matter of the amount of fluid taken during the day. This is comparatively high with the low protein diet, in which the vegetables, cereals and fruits contain much moisture; in the high diet it is forced to some extent, although even here, during hot weather, especially when there is much water lost through the skin, as Lyle and Sharlit have shown, and as is noted in the present observations, the amount of water consumed is inadequate to result in much variation in the amounts of urine eliminated, and the result may be a distinct fixation of specific gravity, though this occurs but rarely, and always at a high level; with the normal diet, however, the results are distinctly different, and there is a marked tendency to a fixation of the specific gravity. Evidently, under ordinary circumstances, the normal individual is in the habit of taking less fluid than when consuming the food which we have been accustomed to use in the low and high diet tests. It has been previously mentioned that a kidney apparently affected by a constant diuretic stimulus of frequently repeated drinks of water of moderate size will exhibit periods of polyuria and oliguria (Table 6 and Chart 2), and that this variation in the specific gravity in the specimens of urine obtained from hour to hour appears to be one of the characteristics of a normally functioning kidney when receiving an adequate supply of water, regardless of the diet. It may be concluded, therefore, that under the conditions of the test a normal urine is one which exhibits a variation of specific gravity of 9 degrees or more. A smaller variation does not necessarily indicate that the kidney is abnormal, provided the specific gravity is high (1.020 or over), but may point to a deficient available supply of water from which to form urine. It may prove itself of value in appropriate cases to use this method to determine whether or not an individual is drinking enough water to meet his bodily demands.

THE VOLUME, SPECIFIC GRAVITY AND CONCENTRATION OF NITROGEN OF THE NIGHT URINE IN NORMAL TESTS

The main error of the former normal standard lay in the fact that the volume of the night urine was thought to be 400 c.c. or less. Lyle and Sharlit have already pointed out that this is incorrect. The present studies (Tables 2, 3, 4 and 5) indicate that the night urine, when the collection of this specimen is begun three hours after supper, and no further food or fluid is taken until the next breakfast, may be as high as 750 c.c., regardless of whether the diet be high, low or normal. If this be true, it necessarily follows that the night urines exhibit lower specific gravities and lower concentrations of nitrogen than was originally thought possible. In judging the night specimen, therefore, only urines exceeding 750 c.c. may be looked on as exhibiting nocturnal

polyuria; the specific gravity figures can only be regarded as of any value, in so far as they may, in some cases, be the maximal concentration of the test; the concentration of nitrogen may be interpreted as normal if it is over 1 per cent., but not necessarily as an indication of diminished renal function, if it is lower.

THE REVISED NORMAL STANDARD

The normal standard, as discussed in the foregoing for the various diets, is summarized in Table 7. It would seem from these tabulations (Tables 2, 3, 4 and 5), with some minor differences as indicated in Table 7, and the very obvious conclusion that a high concentration of salt and nitrogen is less frequent on the low than on the other diets,

TABLE 7.—NORMAL STANDARD FOR TEST MEAL FOR RENAL FUNCTION

	Diet		
	High	Low	Normal
Maximum specific gravity	18+	20+	20+
Degrees variation of specific gravity, usually	9+	9+	No value
Specific gravity of night urine	Of no significance		
Volume c.c. of night urine	750 c.c. or less		
N and NaCl per cent. in night urine or highest per cent. in any specimen	Normal if 1 per cent. or higher, not necessarily abnormal if less		

that the diets may be used interchangeably for the test. When the significance of the factors already discussed is more thoroughly understood, various simpler methods will perhaps be devised to test out one point or the other that may seem especially important. The summary given in Table 7 would indicate that the height of the maximum specific gravity and the volume of the night urine are the most constant features of the normal test, regardless of the diet. The other characteristics are possibly robbed of some, but not all, of their significance, because they fluctuate within such wide limits.

TEST MEALS FOR RENAL FUNCTION ON HIGH AND LOW DIETS IN ABNORMAL INDIVIDUALS

The comparative value of test meals for renal function on high and low diets was observed in 114 patients whose diagnoses are detailed in Table 8. In the study of these cases only the high and low diets were employed. It was thought that these would probably yield results with the greatest possible contrast. "Normal" diets are usually impracticable in the class of patients under consideration. The only possible disturbing element, if other diets than these would be employed in carrying out the test, would appear to be the greater tendency to a

fixation of the specific gravity (Table 5). Due allowance can be readily made for this variation. The tests under consideration are so numerous that only a summary of them can be presented. The findings previously reported[2] for diseases of the urinary tract have been thoroughly substantiated, and only such facts as appear to be new will be completely discussed.

TABLE 8.—CASES IN WHICH A COMPARISON OF TEST MEALS ON HIGH AND LOW DIETS WAS MADE

Diagnosis	Number of Cases
Chronic nephritis	58
Essential hypertension	21
Acute nephritis	13
No renal disturbance	6
Pyelitis and cystitis	4
Cardiac disease	4
Marked anemia	3
Hyperthyroidism	2
Spinal cord injury and paralysis of bladder	1
Polycystic kidneys	1
	114

NOCTURNAL POLYURIA

There were twenty-one patients of the 114 studied in whom there was a nocturnal polyuria (that is, more than 750 c.c. of urine at night) on only one of the tests. It is very significant that the increase of night urine occurred almost exclusively on the high diet (Table 9). In only two of the twenty-one cases in question was it found with the low diet test; in one of these the patient was evidently eliminating edema at the time he was exhibiting a nocturnal polyuria and may therefore be considered as being under diuretic influences, which nullified those of the diet; there was no evident explanation for the occurrence of the increased volume of night urine on the low diet in the second case, the one diagnosed as hypertension.

It is self evident that there should be a greater elimination of salt and nitrogen on the days of the high diet than on the low. This increased excretion is likewise present in the corresponding night urine (Table 9). This simple fact throws much light on the question of nocturnal polyuria, which has thus far been largely accepted as a symptom for which there was no definite explanation. It may be noted that in both instances in which the nocturnal polyuria occurred during the low diet period there was an increased elimination of salt and, in one case, an increased excretion of nitrogen, as compared to the high diet period. It would then appear that the quantity of solids which the kidney was eliminating might be considered the determining factor controlling the amount of night urine. In the first place, it may be concluded that nocturnal polyuria is a compensatory phenomenon to bring about the elimination of solids which a defective kidney

cannot excrete except at lower concentrations than normal; in the second place, it appears that nocturnal polyuria is a signal that the kidney function is being overtaxed and that, in some instances at least, a suitable diet may do away with this unnecessary strain.

TABLE 9.—Comparison of Night Urines in Those Cases in which There Was Nocturnal Polyuria (More Than 750 C.c.) on Only One of the Test Diets.

Diagnosis	Phenol-sulphone-phthalein, Per Cent.	Night Urine					
		Low Diet			High Diet		
		Volume, C.C.	NaCl Gm.	N Gm.	Volume, C.C.	NaCl Gm.	N Gm.
Chronic nephritis	0	720	2.02	3.67	**840**	2.86	4.12
Chronic nephritis	10	475	1.02	2.09	**1055**	4.01	3.69
Chronic nephritis	16	590	2.12	2.42	**825**	3.52	2.87
Chronic nephritis	20	535	2.68	2.14	**1147**	6.07	6.07
Chronic nephritis	31	790	4.22	4.00	**790**	4.66	4.19
Chronic nephritis	32	400	1.28	3.20	**780**	3.30	5.30
Chronic nephritis	37	610	4.03	2.68	**1300**	8.32	4.29
Chronic nephritis	39	470	2.44	1.44	**820**	5.58	4.02
Chronic nephritis	39	**1080**	5.40	3.50	335	2.61	3.47
Chronic nephritis	45	595	1.70	2.92	**1910**	4.39	5.73
Chronic nephritis	46	525	1.10	4.52	**1170**	2.46	4.68
Essential hypertension	63	415	4.07	4.57	**900**	9.18	7.11
Essential hypertension	60	**1040**	4.68	2.70	550	3.58	4.02
Essential hypertension	57	565	4.80	2.88	**787**	5.52	4.60
Essential hypertension	59	725	4.35	2.32	**1240**	9.18	5.08
Acute nephritis	24	440	1.36	2.68	**860**	3.27	5.07
Acute nephritis	35	740	3.26	2.59	**1160**	4.64	4.18
Acute nephritis	61	600	1.65	3.17	**795**	1.91	3.98
Pyelitis and cystitis	65	415	1.83	2.78	**780**	3.98	3.59
Anemia	..	520	2.81	1.82	**1250**	2.75	6.34
Chronic arthritis	75	507	2.26	2.86	**1004**	5.75	4.66

A detailed example of these phenomena is given in Table 10 and Chart 3. This was a case of chronic nephritis of moderate severity. The tests on the low diet and the high diets show absolute agreement except for the presence of nocturnal polyuria on the high diet and none on the low. There is a distinct fixation of specific gravity at a rather low level — ± 1.014; the concentrations for salt and nitrogen do not rise very high and are fairly constant, and the output of fluid during the day is approximately the same in both instances; in the night urine, however, the high diet test shows a volume of 780 c.c., containing 3.2 gm. of sodium chlorid and 5.3 gm. of nitrogen, as con-

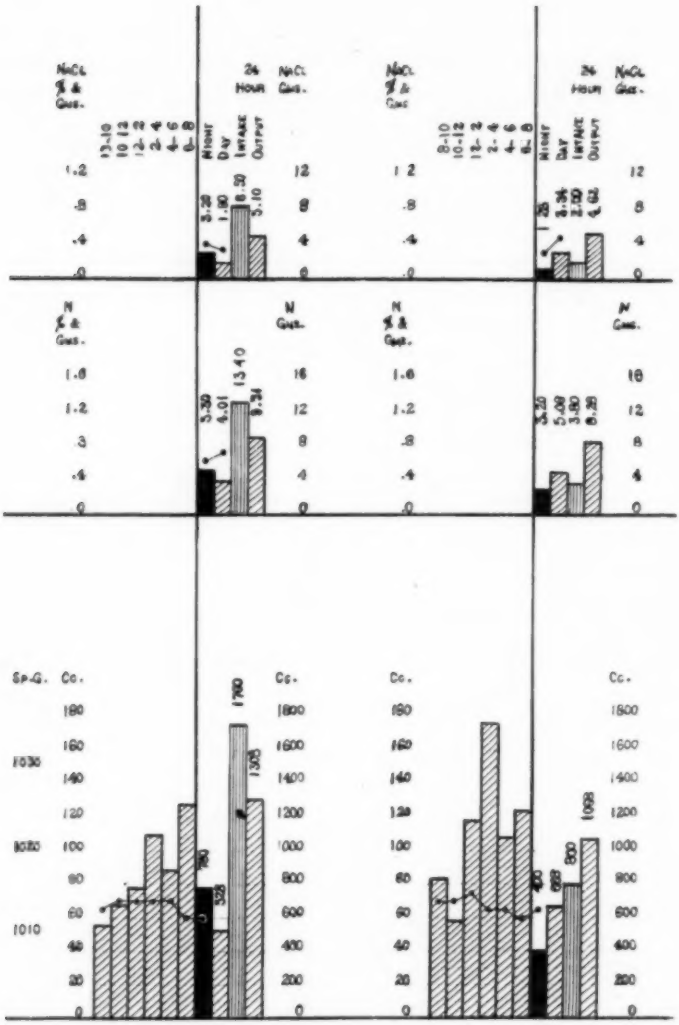
trasted with 400 c.c., sodium chlorid, 1.28 gm., and nitrogen, 3.2 gm., on the low diet. Since the concentrations of sodium chlorid and nitrogen in the urine did not vary appreciably, it would appear that the nocturnal polyuria here is a distinct compensatory manifestation to eliminate the solids which would otherwise have been retained.

TABLE 10.—Results with High and Low Diets in a Case of Chronic Nephritis of Moderate Severity. The Tests Are in Absolute Agreement Except That Nocturnal Polyuria Is Present on the High Diet and Not on the Low Diet. This Is a Very Common Discrepancy. (The Figures Correspond with Chart 3.)

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen		Albumin, Per Cent.
			Per Cent.	Grams	Per Cent.	Grams	
8-10	56	1.013					
10-12	68	1.014					
12- 2	78	1.014					
2- 4	110	1.014					
4- 6	88	1.014					
6- 8	128	1.012					
Total, day....	528	....	0.36	1.90	0.76	4.01	Faint trace
Night, 8-8.....	780	1.012	0.41	3.20	0.68	5.30	Faint trace
Total, 24 hrs..	1,308	....	....	5.10	....	9.31	.....
Intake.....	1,760	....	....	8.50	....	13.40	.....
Balance.....	+452	....	....	+3.40	....	+4.09	.....

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen		Albumin, Per Cent.
			Per Cent.	Grams	Per Cent.	Grams	
8-10	84	1.014					
10-12	58	1.014					
12- 2	118	1.015					
2- 4	176	1.013					
4- 6	108	1 013					
6- 8	124	1.012					
Total, day....	668	....	0.50	3.34	0.76	5.08	Faint trace
Night, 8-8.....	400	1.013	0.32	1.28	0.80	3.20	Faint trace
Total, 24 hrs..	1,068	....	....	4.62	....	8.28	.....
Intake.....	800	....	....	2.00	....	3.80	.....
Balance.....	—268	....	....	—2.62	....	—4.48	.....

It has been generally believed that polyuria, in chronic nephritis and other conditions, is a favorable symptom, provided that it results in an adequate excretion of solids in the urine, and dietetic measures have as a rule not been directed against it. In diabetes insipidus we



High Diet Test Low Diet Test

Chart 3.—Results with high and low diets in a case of chronic nephritis of moderate severity. The tests are in absolute agreement except that nocturnal polyuria is present on the high diet and not on the low diet. This is a very common discrepancy.

have an example of the most extreme polyuria which apparently does not damage the kidney. Cases of chronic nephritis, however, present a different problem; in them it may very well be that overstrain of the function of water excretion may result in further damage to the kidneys. While the present observations do not furnish conclusive evidence on this point, it is interesting to note that many of these patients welcomed the low protein diet because it relieved their thirst to such a great degree. To them the polyuria appeared to be a secondary consideration. Furthermore, in one instance, at least, an accidental observation showed that water given in large amounts may result in a diminished urinary output instead of an increase (Chart 4). Similar phenomena have been recorded as the result of diuretic drugs and sodium chlorid. That a diuretic as bland as water should "fatigue" the kidney is probably somewhat surprising. In another instance of severe nephritis, the same phenomenon was seen as the result of a glucose infusion. It may be that a polyuria persisting for a longer period may cause a gradual impairment of renal function, just as the sudden huge increase of water intake in the instances cited in the foregoing brought about an immediate diminution in the volume of urine. These facts must be looked on as suggestive only, unless they are borne out by further evidence. There were nine cases of chronic nephritis in the present series exhibiting nocturnal polyuria on both diets; their phenolsulphonephthalein excretion ranged from 35 to 5. The eleven cases in which the abnormally high night urine was present on only one diet (almost invariably on the high diet, Table 9) showed a phenolsulphonephthalein varying from 46 to 0. The remaining cases of chronic nephritis, thirty-eight in number, in which there was a night urine, normal in amount, on both the high and the low diets, revealed phenolsulphonephthalein excretions varying from 0 to 58 per cent. in two hours. Of the twenty-one cases classified as hypertension, in which the phenolsulphonephthalein was approximately normal, there was nocturnal polyuria on the low diet in one case, on the high diet in three cases, and no nocturnal polyuria on either diet in seventeen cases. From these facts it may be concluded that nocturnal polyuria may be absent even when there is a very marked renal insufficiency, but that when it is present it indicates a distinct impairment of function, especially if the night urine is increased while the patient is on a low diet.

As has been stated before, the interpretation and therapy of any one of these abnormalities depend largely on the cause. An entirely different significance is to be attributed to nocturnal polyuria in chronic and acute nephritis, pyelitis, cystitis, severe anemia, diabetes insipidus, etc. In general, nocturnal polyuria was found to exist in the same type of cases as in the observations previously recorded.

THE MAXIMAL SPECIFIC GRAVITY

This is probably one of the most important features in measuring renal function by the method under consideration. It has been previously noted how, as the activity of the kidney becomes impaired, there is a tendency for the specific gravity of the urine to assume a lower level until in the final stages it usually cannot be raised above 1.010. In the present studies it has been shown that in the normal individual the test meal for renal function elicits a maximal specific gravity of 1.018 or over on the high diet and of 1.020 or more on the low (Table 5). In comparing the results of the high and low diet, as far as the maximal specific gravities are concerned, in abnormal individuals, there is a fairly close agreement (Table 11).

As is shown by the figures in heavy type in the comparative statistics given in Table 11, there is more than a very slight disagreement in the conclusion to be drawn from the maximal specific gravity on the high and low diets in only sixteen out of the 114 tests, and in most of these the difference is not very great. There are, however, a few in which there is a marked divergence between the two. In a number of these it is the very rapid change which renal function undergoes in patients in whom there is an edema, either because of passive congestion brought on by myocardial insufficiency, or as an accompaniment of either chronic or acute nephritis. In all of these conditions, which are so closely related to the question of renal function, both in chronic and acute nephritis, there is nearly always a specific gravity of about 1.020, which is usually fairly fixed. The change from an oliguric state to one in which there is a polyuria and an elimination of the retained fluid, is often, though not always, a very rapid one. This very sudden increase in the quantity of urine elimination is accompanied by a corresponding depression in the specific gravity. This, instead of being constantly high, now becomes fixed at a low level. In two cases, a record of the urinary excretion by the test meal method was fortunately obtained on the day when the polyuria set in. In the first patient there had been a very marked and persistent edema for more than four months; he was suffering with an acute nephritis which was becoming chronic. Table 12 and Chart 5 show how rapidly in his case the transformation occurred from one specimen to the next; it may be considered to be a matter of minutes only. Another patient, a case of acute nephritis, exhibited this same sudden remarkable change (Table 13). It is probable that most of the very marked differences occurring in maximal specific gravities of the high and low test meals are accounted for in this way. The findings in regard to the above phenomenon have been so constant that from a single specimen it was often

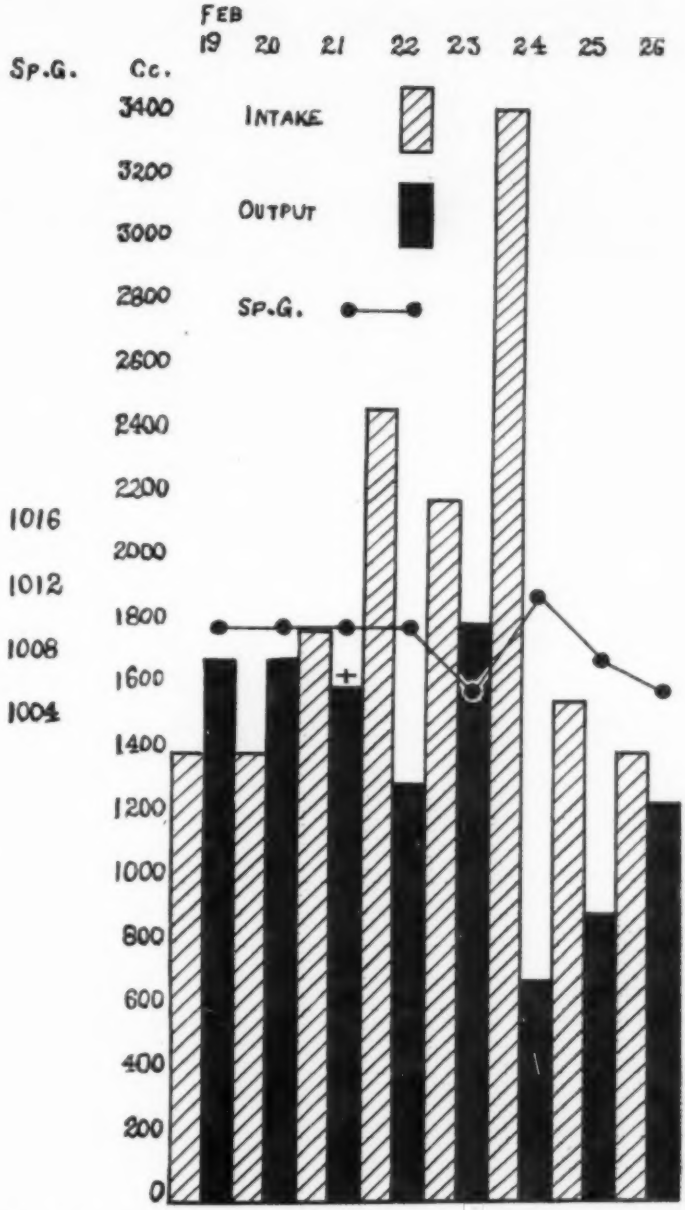


Chart 4.—The result of forcing fluids in a case of marked chronic nephritis. (The low, fixed specific gravity is seen in the chart, the phenolsulphonephthalein excretion was 5 per cent. in two hours.) The large fluid intake did not bring about an increased output of urine, but evidently had the opposite effect, indicating that what we consider to be the blandest of all diuretics, water, may, if given in excess, cause further impairment of renal function in severe nephritis.

TABLE 11.—Comparison of the Maximal Specific Gravities Obtained on the High and Low Diets in Abnormal Persons*

Diagnosis	Number of Cases in which Both Tests Are Normal†	Cases in which the Maximal Specific Gravity is Below Normal in One Test Only			Cases in which the Maximal Specific Gravity is Below Normal in Both Tests		
		Maximal Specific Gravity‡		Phenolsulphonephthalein Per Cent. in Two Hours	Maximal Specific Gravity§		Phenolsulphonephthalein Per Cent. in Two Hours
		Low Diet	High Diet		Low Diet	High Diet	
Chronic nephritis	16	**(16)**	21	65	12	16	60
		(18)	19	55	15	12	58
		29	(17)	53	18	15	46
		22	**(14)**	47	**14**	**09**	46
		(19)	22	44	15	16	45
		22	(17)	41	17	15	45
		(18)	20	41	17	15	44
		(19)	19	37	**16**	**11**	40
		(19)	18	30	11	11	36
		(17)	18	29	09	12	35
					19	**15**	34
					15	14	32
					14	15	31
					12	12	30
					15	15	30
					14	13	29
					19	17	21
					11	10	20
					12	12	20
					13	12	20
					13	12	20
					14	17	16
					10	11	16
					16	17	12
					10	11	10
					14	11	10
					10	09	8
					10	12	5
					10	08	5
					08	09	5
					10	11	0
					13	14	0
Acute nephritis	0	**(17)**	19	72	09	12	61
		(14)	21	50	14	14	60
		(15)	18	34	13	12	54
					16	17	54
					16	15	53
					13	15	50
					15	15	40
					15	15	35
					17	15	35
					13	14	24
Essential hypertension	11	20	**(17)**	69	14	17	81
		(15)	18	68	**19**	**15**	59
		(10)	20	67	15	15	49
		(19)	20	65			
		21	**(14)**	57			
		(19)	20	51			
		(14)	18	46			
Polycystic kidneys	0	....	....	..	10	10	0
Cystitis and pyelitis	1	....	....	..	10	11	60
		(17)	19	76	09	11	57
Cardiac disease	2	(19)	26	60			
		(19)	25	31			
Anemia	1	26	**(15)**	55	12	14	73
Hyperthyroidism	2	....	....	..	17	17	
Spinal cord lesion and bladder paralysis	0	....	....	..	14	12	0
No renal lesion	3	25	(17)	75	19	17	68
		29	(17)	72			

* Only the last two figures of the specific gravity are charted.

† 1018+, on high diet; 1020+, on low diet.

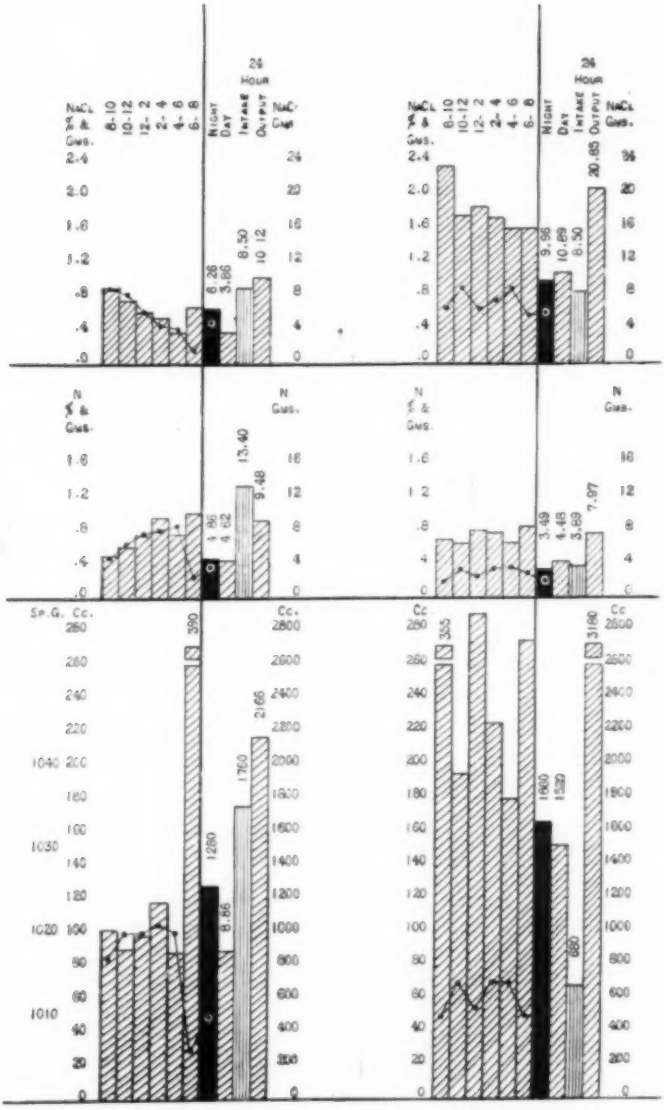
‡ The figure in parenthesis is the abnormal one. Instances in which the abnormal figure is more than 2 points below normal are printed in heavy type.

§ Instances in which the variation between the maximal figures of the two diets is .4 or over are printed in heavy type.

TABLE 12.—Results in a Case of Acute Nephritis with Edema. The Edema Had Persisted for About Four Months. On the Day of High Diet the Very Sudden Change to Polyuria with a Much Lowered Specific Gravity May Be Noted. On the Low Diet the Marked Success of the Kidney in Eliminating Edema Is Evident. These Changes in Edematous Cases Frequently Are Responsible for Very Varying Results. (The Figures Correspond with Chart 5.)

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen	
			Per Cent.	Grams	Per Cent.	Grams
8-10	102	1.017	0.89	0.91	0.50	0.51
10-12	90	1.020	0.83	0.75	0.68	0.61
12- 2	98	1.020	0.63	0.62	0.78	0.76
2- 4	118	1.021	0.47	0.55	0.81	0.96
4- 6	88	1.020	0.42	0.37	0.88	0.77
6- 8	390	1.006	0.17	0.66	0.26	1.01
Total, day.....	886	....	....	3.86	....	4.62
Night, 8-8.....	1,280	1.010	0.49	6.26	0.38	4.86
Total, 24 hrs....	2,166	....	....	10.12	....	9.48
Intake.....	1,760	....	....	8.50	....	13.40
Balance.....	—406	....	....	—1.62	....	+3.92

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen	
			Per Cent.	Grams	Per Cent.	Grams
8-10	355	1.010	0.66	2.34	0.20	0.71
10-12	195	1.014	0.90	1.76	0.34	0.66
12- 2	290	1.011	0.64	1.86	0.28	0.81
2- 4	225	1.014	0.77	1.73	0.35	0.79
4- 6	180	1.014	0.89	1.60	0.37	0.67
6- 8	275	1.010	0.58	1.60	0.31	0.85
Total, day.....	1,520	....	....	10.89	....	4.48
Night, 8-8.....	1,660	1.010	0.60	9.96	0.21	3.49
Total, 24 hrs....	3,180	....	....	20.85	....	7.97
Intake.....	680	....	....	8.50	....	3.80
Balance.....	—2,500	....	....	—12.35	....	—4.08



High Diet Test Low Diet Test

Chart 5.—Results in a case of acute nephritis with edema. The edema had persisted for about four months. On the day of high diet the very sudden change to polyuria with a much lowered specific gravity may be noted. On the low diet the marked success of the kidney in eliminating edema is evident. These changes in edematous cases frequently are responsible for very varying results.

possible to determine whether the edema was retained (specific gravity ± 1.020) or eliminated (specific gravity ± 1.010).

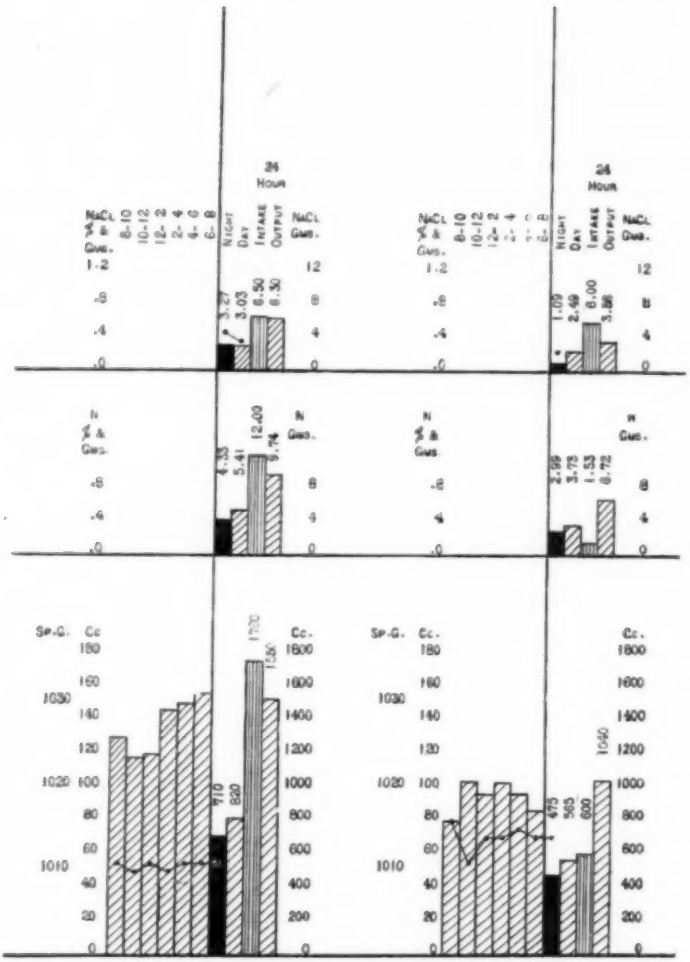
At times this transition from a marked oliguria to a pronounced polyuria is not so abrupt. The case of which tests are given in Table 14 and Chart 6 illustrates this. This was a patient afflicted with a marked chronic nephritis, accompanied by a moderate degree of edema. There is no very marked difference between the two tests except that on the day of high diet the specific gravity was fixed at a lower level (± 1.011) than on the low (± 1.014).

TABLE 13.—Result of Test Meal on High Diet in a Case of Acute Nephritis. The Sharp Change from Oliguria with a High Specific Gravity to Polyuria and a Low Specific Gravity Is Striking. This Is Presumably the Exact Time at which the Kidneys Began to Eliminate the Edema.

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen	
			Per Cent.	Grams	Per Cent.	Grams
8-10	40	1.021				
10-12	63	1.021				
12- 2	85	1.020				
2- 4	57	1.018				
4- 6	88	1.017				
6- 8	228	1.009				
Total, day.....	506	....	0.57	2.86	0.66	3.34
Night, 8-8.....	1,228	1.010	0.50	6.14	0.33	4.05
Total, 24 hrs....	1,734	....	....	9.02	....	7.39
Intake.....	1,760	....	....	3.00	....	13.40
Balance.....	+26	....	....	−6.02	....	+6.01

This would seem to indicate that fluid was being more readily eliminated in the first period. There is not much difference in the fluid balances of the two days. (It has already been noted how on the low diet, because of the fluid contained in the vegetables, fruits and the boiled cereals and puddings, there is an apparently negative fluid balance in normal individuals. The small water loss on the low diet day may, therefore, be considered to be within normal limits). It is probable, however, that the retention of fluid was responsible for the test in which the specific gravity was 1.014 and that the elimination of the edema resulted in the urinary specimens with a specific gravity of 1.011.

It must be borne in mind in this connection that cases of very severe nephritis may not show an elevation of the specific gravity in spite of a failing heart and congestion of the kidneys, or because of the accumulation of edema associated with renal disease. These



High Diet Test Low Diet Test

Chart 6.—Results with high and low diets in an advanced case of chronic nephritis with edema. It is probable that the varying reaction of the kidney to the retained fluid is responsible for the difference in the two tests. Here the changes are not as abrupt as in Tables 12 and 13. The maximal specific gravity on the low diet is moderately lower than normal; that on the high diet is markedly so.

are among the most advanced types of diminished renal function met with, and in them the maximal specific gravity is always at a level of about 1.010. This accounts for the very marked agreement of the

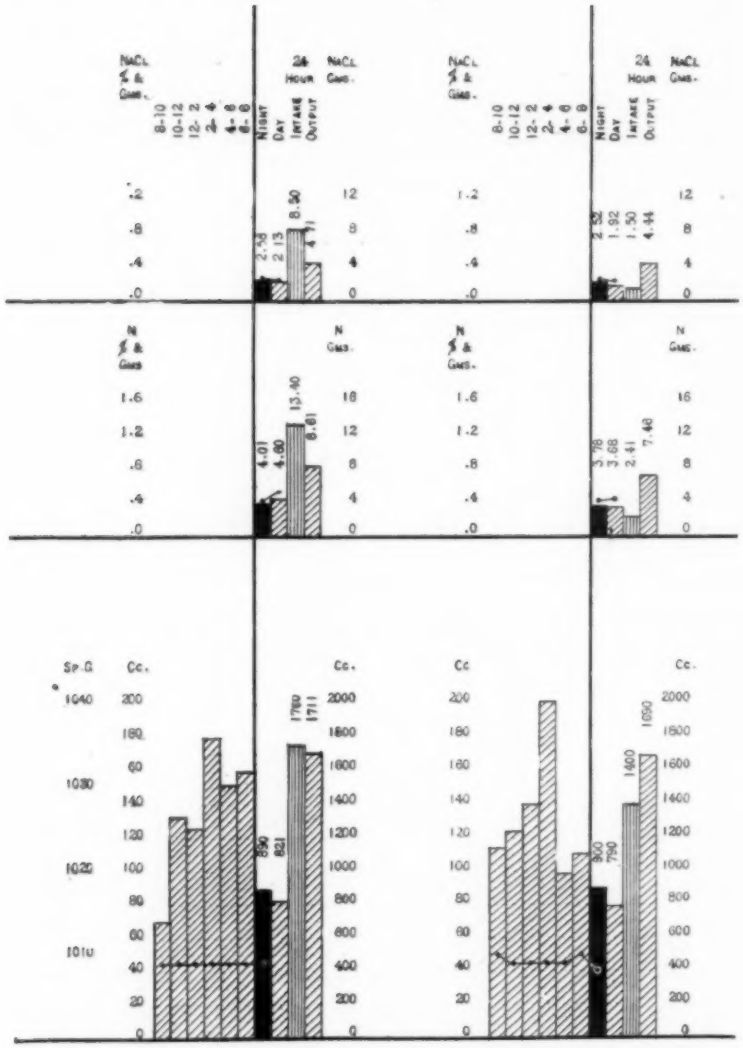
TABLE 14.—Results with High and Low Diets in an Advanced Case of Chronic Nephritis with Edema. The Maximal Specific Gravity on the Low Diet Is Moderately Lower Than Normal, That on the High Diet Is Markedly So. (The Figures Correspond with Chart 6.)

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen	
			Per Cent.	Grams	Per Cent.	Grams
8-10	130	1.011				
10-12	118	1.010				
12- 2	120	1.011				
2- 4	146	1.019				
4- 6	150	1.011				
6- 8	156	1.011				
Total, day.....	820	....	0.37	3.03	0.66	5.41
Night, 8-8.....	710	1.011	0.46	3.27	0.61	4.33
Total, 24 hrs....	1,530	....	....	6.30	....	9.74
Intake.....	1,760	....	....	6.50	....	12.00
Balance.....	+230	....	....	+0.20	....	+2.26

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen	
			Per Cent.	Grams	Per Cent.	Grams
8-10	80	1.016				
10-12	104	1.011				
12- 2	96	1.014				
2- 4	103	1.014				
4- 6	96	1.015				
6- 8	86	1.014				
Total, day.....	565	....	0.44	2.49	0.66	3.73
Night, 8-8.....	475	1.014	0.23	1.09	0.63	2.99
Total, 24 hrs....	1,040	....	....	3.58	....	6.72
Intake.....	600	....	....	6.00	....	1.53
Balance.....	−440	....	....	+2.42	....	−5.19

maximal specific gravity figures for the two tests found in most of the cases with a very low phenolsulphonephthalein excretion (Table 11). The results of the tests in a case of this sort are furnished in Table 15, Chart 7. The results of the two tests are almost identical in every respect. Other tests were made on this patient at various intervals and always yielded similar results.

It may, therefore, be concluded that the maximal specific gravity values obtained with the low and the high diets are of equal signifi-



High Diet Test Low Diet Test

Chart 7.—Results with high and low diets in a case of nephritis of maximal severity; there is absolute agreement between the two tests. In this patient neither the occurrence of a transient myocardial insufficiency nor the temporary presence of a moderate grade of edema changed the results obtained at various times.

cance; that variations may occur but that these are usually caused by the alternate retention or elimination of edematous fluid, and are apparently not influenced by the character of the test diet. Changes in the level of the specific gravity, as the result of such a deranged water metabolism, may be extremely rapid or may occur very gradually.

TABLE 15.—Results with High and Low Diets in a Case of Nephritis of Maximal Severity; There Is Absolute Agreement Between the Two Tests. In This Patient Neither the Occurrence of a Transient Myocardial Insufficiency Nor the Temporary Presence of a Moderate Grade of Edema Changed the Results Obtained at Various Times. (The Figures Correspond with Chart 7.)

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen		Albumin, Per Cent.
			Per Cent.	Grams	Per Cent.	Grams	
8-10	70	1.009					
10-12	133	1.009					
12- 2	126	1.009					
2- 4	180	1.009					
4- 6	152	1.009					
6- 8	160	1.009					
Total, day.....	821	....	0.26	2.13	0.56	4.60	1.0
Night, 8-8.....	890	1.009	0.29	2.58	0.45	4.01	0.8
Total, 24 hrs....	1,711	....	....	4.71	....	8.61	...
Intake.....	1,760	....	....	8.50	....	13.40	...
Balance.....	+49	....	....	+3.79	....	+4.79	...

Time of Day	C.C.	Specific Gravity	Sodium Chlorid		Nitrogen		Albumin, Per Cent.
			Per Cent.	Grams	Per Cent.	Grams	
8-10	114	1.010					
10-12	124	1.009					
12- 2	140	1.009					
2- 4	204	1.009					
4- 6	98	1.009					
6- 8	110	1.010					
Total, day.....	790	....	0.24	1.92	0.48	3.68	1.0
Night, 8-8.....	900	1.008	0.28	2.52	0.42	3.78	0.8
Total, 24 hrs....	1,690	....	....	4.44	....	7.46	...
Intake.....	1,400	....	....	1.50	....	2.41	...
Balance.....	−290	....	....	−2.94	....	−5.05	...

THE VARIATION OF SPECIFIC GRAVITY

A study of Table 16 shows that there is no great divergence in the degrees of variation in the specific gravity readings on the high and low diets in abnormal individuals. Of the fifty-six tests exhibiting a subnormal variation on both diets, there are only seven (figures in

heavy type in Table 16) in which the difference between the high and low diets indicated a marked discrepancy. Of those exhibiting a subnormal divergence on only one diet, it appears that an impairment of renal function (figures in heavy type, Table 16) is more frequently manifested on the high (sixteen instances) than on the low diet (nine instances). The reason for this is probably to be found in the relatively greater intake of fluid in proportion to the solid food in the low diet.

The same factors that may cause a fixation of specific gravity in the normal individual (as previously discussed) may also be considered to apply to the abnormal. However, the subject whose renal function is not impaired usually shows a fixation of specific gravity at a high level, while with an impairment of renal function this manifests itself at a much lower point (Table 16). It must be borne in mind that cases of passive congestion of the kidneys and cases of oliguria in either acute or chronic nephritis may all have a tendency to fix their specific gravity at about 1.020. That a low, fixed specific gravity does not admit of one interpretation but must be closely correlated with the clinical findings, may be readily gathered from Table 16. It is obvious that this symptom has an entirely different significance in chronic nephritis with a low phenolsulphonephthalein output than it has in acute nephritis or cystitis when the phenolsulphonephthalein excretion is normal or nearly so.

The marked variations that occurred in some of the cases may be largely explained, as were the differences in maximal specific gravity readings on the low and high diets, by sudden or more gradual changes in the response of the kidney to edema. Tables 12, 13 and 14, and Charts 5 and 6 illustrate this very well.

It may be concluded, therefore, that the degree of variation of specific gravity in test meals for renal function is not very different, whether high or low diets be employed.

SUMMARY

Specimens of urine were collected at two-hourly intervals during the day and for a twelve-hour period at night in a considerable number of normal subjects. Various diets were employed while these tests were carried out. It appears that certain characteristics, as indicated by the specific gravity of all the specimens and the volume of the night urine, are present regardless of the diet. These are summarized in Tables 5 and 7, and they may be regarded as the normal standards by which to judge similar tests in abnormal individuals.

A normal individual will void very varying two-hourly specimens, even though the intake of food and fluid is restricted to constant

TABLE 16.—Comparison of the Degrees of Variation of Secific Gravity on the High and Low Diets in Abnormal Persons

Diagnosis	Number of Cases with a Variation of 9 Degrees or More on Both Tests	Cases with a Variation of Less than 9 in One Test Only				Cases with a Variation of Less than 9 in Both Tests			
		Degrees Variation Specific Gravity*		Maximal Specific Gravity of Test Showing Least Variation	Phenol-sulphone-phthalein Per Cent. in Two Hours	Degrees Variation Specific Gravity†		Maximal Specific Gravity of Test Showing Least Variation	Phenol-sulphone-phthalein Per Cent. in Two Hours
		Low Diet	High Diet			Low Diet	High Diet		
Chronic nephritis	17	**8**	10	29	53	**8**	**3**	12	56
		12	7	15	46	8	7	22	47
		10	**3**	09	46	5	8	10	40
		10	7	16	45	**5**	**1**	11	40
		13	**6**	15	44	7	4	13	39
		10	4	18	39	6	7	20	38
		7	14	30	35	8	9	19	37
		9	**6**	18	30	4	3	11	36
						2	3	09	35
						6	**2**	15	35
						3	2	14	32
						4	3	15	31
						2	**7**	20	31
						2	3	15	30
						6	7	12	30
						5	7	17	29
						5	5	22	25
						4	2	12	21
						4	5	19	21
						4	2	11	20
						5	**1**	10	20
						2	3	10	16
						2	4	14	16
						2	3	16	12
						6	**1**	11	10
						2	1	11	10
						2	0	09	8
						3	3	10	5
						*	0	08	5
						2	1	08	5
						5	**1**	14	5
						3	4	12	0
						2	1	11	0
Acute nephritis	1	**6**	12	17	72	1	2	09	61
		13	**6**	16	54	5	8	14	60
		4	15	14	50	1	2	13	54
						3	5	16	53
						8	6	16	50
						4	3	15	40
						3	5	15	35
						5	2	15	35
						2	3	13	24
Essential hypertension	6	**8**	12	14	81	7	6	17	79
		9	**5**	24	78	7	7	10	67
		9	7	18	68	6	6	13	60
		13	**6**	20	65	6	5	20	55
		13	7	15	59	5	4	24	54
		16	**8**	14	57	5	2	29	54
		8	15	18	55				
		12	**5**	25	52				
		6	11	19	51				
Polycystic kidneys	6	..	..	..	..	0	1	10	0
Cystitis and pyelitis	2	..	..	..	..	2	1	11	60
						6	**5**	09	57
Cardiac disease	1	17	7	33	55	7	6	21	40
						8	7	19	31
Anemia	1	17	**8**	15	55	4	3	12	73
Hyperthyroidism	1	1	14	28	..	4	7	17	..
Spinal cord lesion and bladder paralysis	9	..	..	..	..	1	1	12	0
No renal lesion	4	13	7	17	75				
		6	11	24	58				

* The figures in heavy type indicate the test in which the variation is less than 9.

† The figures in heavy type indicate the comparative tests in which there was a marked difference (more than 3 degrees) in the variation on the low and high diets.

quantities of water taken at two-hourly intervals. Under these circumstances there are periods of polyuria with a rather low specific gravity, alternating with oliguria and a higher specific gravity. This phenomenon may prove to be a criterion of the amount of fluid necessary to carry on the vital activities of the body. If only small amounts are taken, the urine output is low, constant from one two-hour period to the next, and the specific gravity becomes fixed at a fairly high level.

Comparative tests on fairly high and low protein diets were carried out in a series of patients afflicted with various diseases that are known to impair renal function. It was found that in the main the results agreed regardless of the diet. Nocturnal polyuria was more frequent on the high than on the low diet. This was evidently due to an effort on the part of the kidney to eliminate solids by means of polyuria when an adequate concentration of solids was no longer possible. Nocturnal polyuria, when occurring with a low protein diet, must therefore be regarded as a much graver sign of renal insufficiency than when it occurs with a high protein intake.

Marked variations in the results were brought about by the elimination of edema. When edema is present, the change from oliguria to polyuria may come about with extreme rapidity and influence the interpretation of renal function, if judged by the urine alone and not by the clinical aspects of the case as well. In every instance, as has been previously accentuated, the urinary findings must be correlated with the character of the diseased processes giving rise to the changes in the kidneys, in order that the exact significance of this test for renal fnuction may be appreciated.

TACHYCARDIA OF UNKNOWN ORIGIN*

THEODORE B. BARRINGER, JR., M.D.
NEW YORK

Among the draft registrants examined during the spring of 1918 by the New York Hospital medical advisory boards there were 141 men with organic heart disease and ninety-three with what we will describe briefly as "tachycardias of unknown origin." Further scrutiny of this latter group would probably have shown that a small number were early cases of Graves' disease (exophthalmic goiter) or tuberculosis, and that alcohol was the cause of the rapid heart rate in another small group. A surprisingly large proportion of the men suffering from circulatory disease, however, would be found in this group of what we have termed, for want of a better name, "tachycardias of unknown origin."

Fourteen of these men were examined a number of times, their histories being taken carefully and their circulatory reactions to graduated work being determined on at least three occasions. Chief importance will be attached to our objective findings, for many of these men either believed that they were not physically fitted for army service or wished to avoid such service, which did not tend to increase the reliability of their histories. Our experiments with graduated work led us to classify our fourteen cases into two groups — a severe type and a mild type. The reasons for this classification will be given later.

FAMILY HISTORIES

Six of our patients gave a history of neurotic taint in the family.

S. R., aged 21; severe type of case; mother hysterical; father of violent temper; one sister nervous; one brother has pulmonary tuberculosis.

S. B., aged 23; severe type of case; mother died of melancholia; one sister has melancholia.

C. G., aged 22; moderate type of case; mother epileptic.

F. S., aged 28; mild type of case; mother has melancholia, "nervous prostration" and pulmonary tuberculosis.

A. S., aged 22; mild type of case; mother has "nervous prostration" and hysterical attacks.

S. F., aged 22; mild case; father's father insane; mother is nervous and has rapid heart action.

* Submitted for publication June 19, 1918.

HISTORY OF INFECTION

In no one of our five severe cases had the patient ever had acute articular rheumatism; one had had scarlet fever and another diphtheria.

The patients in nine mild or moderate cases gave no history of acute articular rheumatism; two had had scarlet fever and one had had three attacks of pneumonia.

NATURE AND TIME OF ONSET OF SYMPTOMS

Severe Type of Case.—P. P., for eight years has had pain around the heart, exhaustion and shortness of breath after exercise.

S. R., when a small boy couldn't play with other boys on account of shortness of breath. For five years he has suffered from palpitation and pain around the heart following exercise.

S. B., for three years has had palpitation and breathlessness after exercising.

P. R., when a child could not run on account of shortness of breath and cardiac pain. These symptoms, evoked by exercise, have persisted.

A. V., when a small boy had to stop running before his comrades did on account of shortness of breath. Has had rapid heart action for the past fourteen years.

Mild Type of Case.—Two of these nine mild cases gave histories of breathlessness on exertion beginning in childhood. One of these histories was probably false. The other seven men complained of breathlessness on exertion and palpitation or rapid heart action beginning from one to six years previously.

One man (S. F.) occasionally had a stinging pain over the heart after exercise and another (K. X.) complained of substernal pain after exercise.

Nine men said that they disliked whisky, one saying that it made his heart beat more rapidly and caused a choking sensation.

The physical examination of the circulatory systems was normal in all these cases. Occasionally a functional systolic murmur was heard over one of the valvular orifices. The lungs were negative and there was no evidence of exophthalmic goiter.

METHOD OF EXAMINATION

Each man rested sitting on a chair until the pulse rate became constant. Work was furnished by swinging dumb-bells weighing 10, 20 or 25 pounds. The same rhythm was maintained in swinging the bells and work was augmented by increasing the number of swings. Between the exercises the subjects rested for five or ten minutes.

From three to six groups of exercises were given on each day the patient was examined. The men were seen from three to twelve times, several days or a week intervening between the visits.

The pulse was counted in a number of instances immediately after work for fifteen seconds, and in all cases, after 110 seconds had elapsed, for twenty seconds. Thereby the rates immediately after work and at the end of 120 seconds were computed.

The blood pressures were read by the same observer by auscultation, using a Riva-Rocci type of sphygmomanometer. The frequent method[1] of observation was used in every experiment, and the infrequent method[1] in many instances.

REACTIONS TO EXERCISE, CIRCULATORY AND OTHERWISE

Severe Type.—There was a small group of men who responded to exercise in a way quite different from normal individuals. In the first place they were able to do much less work than normal men. Their upper limit of work varied between 1,600 and 4,500 foot-pounds performed in the manner previously described, whereas the normal upper limit at 20 to 30 years of age we have found to be between 6,000 and 12,000 foot-pounds. Again, when they reached the comparatively low limits of their efforts they became dyspneic, exhausted and in three instances complained of precordial pain. When a normal person reaches his limit of work his dyspnea may be quite as marked, but his fatigue is rarely as pronounced and persistent as in these cases. The precordial pain is also a symptom rarely found in normal persons.

The facial expression of these persons when they had finished the heaviest work was anxious and indicated unmistakeably the distress they felt. The precordial pain was referred to the region below the left nipple and was accompanied by tenderness on pressure of the underlying intercostal muscles.

The production by relatively small amounts of work of the syndrome of symptoms just described is, we believe, of more value in determining the severity of the case than are the pulse rate and blood pressure reactions. This has, accordingly, been our chief guide in classifying our cases.

The reactions of the pulse rate are summarized for both severe and mild cases in Table 1 and those of the systolic blood pressure in Table 2. In Table 1 the expression "overtaxed" signifies that the person suffered from marked dyspnea, fatigue or exhaustion and, in severe cases, from precordial pain.

The pulse rates of the severe type of cases were all higher than normal and all showed greater increases immediately after work than

1. Barringer, T. B., Jr.: Am. Jour. Med. Sc., 1918, **155,** 864.

TABLE 1.—Reactions of Pulse Rate to Graduated Work in Cases of Tachycardia

Name and Age	Type of Case	Work in Foot-Pounds	Pulse Rate			Return to Normal in Sec.	Remarks
			Before Work	After Work			
				Immediately	At 120 Sec.		
P. P. 22	Severe	1,600	104	144	116	180	
		(10 s.20) 2,100	100	144	110	150	Overtaxed*
		1,200	116	132	114	120	
		1,800	114	130	124	180	Overtaxed
		(10 s.25) 3,000	112	...	108	120	Overtaxed
		1,200	92	...	108	180	
		1,800	92	...	99	180	
		3,000	92	...	108	180	Overtaxed
		(10 s.30) 3,600	92	...	112	180	Overtaxed
S. R. 21	Severe	2,000	130	142	108		
		3,000	122	144	128		
		(20 s.20) 4,000	112	136	126	180	Overtaxed
		2,000	112	...	140	180	
		2,300	118	...	130	180	
		3,000	112	...	132	240	Overtaxed
		2,100	102	...	108		
		3,000	104	...	118	180	
		(20 s.20) 4,000	100	...	114	180	Overtaxed
P. R. 23	Severe	2,000	96	...	92		
		(20 s.15) 3,000	96	...	112	180	Oxertaxed
		2,000	80	...	100	180	
		3,000	80	...	102	180	Overtaxed
S. B. 23	Severe	2,300	124	148	128		
		3,400	128	180	132	...	Overtaxed
		2,300	136	148	136		
		3,400	136	156	136	...	Overtaxed
		2,300	88	...	120	240	
		3,400	92	...	116	420	Overtaxed
		(20 s.20) 4,000	88	...	104	300	Overtaxed
A. V.	Severe	2,300	92	120	104	180	
		3,400	96	136	100	...	Overtaxed
		(20 s.20) 4,600	96	160	112	240	Overtaxed
		2,300	92	132	92		
		3,400	96	160	116	240	Overtaxed
		4,500	100	...	105		
		6,800	108	...	114		
		7,700	100	...	117	180	Overtaxed
		6,600	100	...	108		
		7,900	100	...	108		
		(25 s.35) 9,200	102	...	100	...	Overtaxed
		6,600	90	...	108		
		7,900	104	...	117	180	Overtaxed
		9,200	102	...	112	180	Overtaxed
K. X. 27	Moderate	3,700	124	...	120		
		5,000	124	...	136	240	Overtaxed
		(25 s.20) 5,500	128	...	130	...	Overtaxed
		4,000	116	...	124	420	
		5,200	128	...	136	200	Overtaxed
		(25 s.25) 7,000	120	...	136	240	Overtaxed

* "Overtaxed" signifies that patient suffered from dyspnea, fatigue or exhaustion and, in some cases, precordial pain. "10 s.20" signifies a 10-pound bell swung twenty times.

TABLE 1.—Reactions of Pulse Rate to Graduated Work in Cases of Tachycardia—(*Continued*)

Name and Age	Type of Case	Work in Foot-Pounds	Pulse Rate			Return to Normal in Sec.	Remarks
			Before Work	After Work			
				Immediately	At 120 Sec.		
C. G. 22	moderate	3,100	96	...	100		
		(20 s.20) 4,000	96	...	102		
		3,100	100	...	100		
		4,000	92	...	118	180	
		(20 s.25) 5,000	88	...	96	...	Overtaxed
P. R. 23	Mild	6,000	104	160	114	180	
		7,000	104	...	120	240	Overtaxed
		8,000	104	...	140	240	Overtaxed
		2,100	112	148	120	180	
		5,100	116	160	128	300	
		5,300	112	160	124	300	Overtaxed
		6,000	84	...	105	180	
		9,000	100	...	120	180	
		10,000	104	...	...	300	Sl. overtaxed
		6,000	90	...	120	300	
		7,500	104	...	124	240	
		9,000	108	...	160	300	Overtaxed
W. R. 25	Mild	3,000	112	148	120	180	
		5,400	116	...	116		
		6,700	112	...	132	240	Overtaxed
		7,000	112	...	136	240	Overtaxed
		5,400	100	...	129	280	
		6,700	100	...	140	240	
		7,000	100	...	132	420	Overtaxed
S. F. 22	Mild	5,100	76	...	88	240	
		7,700	90	...	100	180	Overtaxed
		5,100	84	...	105	300	Sl. overtaxed
		6,100	92	...	102	180	Overtaxed
A. S. 22	Mild	6,300	88	...	92		
		9,400	92	152	120	180	
		10,600	100	...	132	300	Overtaxed
		6,300	104	...	129	300	
		9,400	100	...	135	360	
		11,000	112	...	135	240	Overtaxed
F. M. 23	Mild	4,700	92	112	96		
		5,300	96	112	108	180	Overtaxed
		9,300	88	136	104	240	Overtaxed
		5,300	88	120	88	...	Overtaxed
		9,300	92	144	104	180	Overtaxed
L. H. 22	Mild	2,400	96	136	104		
		3,500	92	140	120	180	Sl. overtaxed
		4,800	92	160	124	240	Overtaxed
		3,500	100	120	104		
		4,500	108	144	112		
		5,300	108	156	120	180	Overtaxed

TABLE 2.—Reactions of Systolic Blood Pressure to Graduated Work in Cases of Tachycardia

Name and Age	Type of Case	Work in Foot-Pounds	Systolic Blood Pressure				Remarks
			Before Work	After Work			
				First Reading	Maximum Reading	Delayed Rise	
P. P. 22	Severe	1,200	122	126	146	No	
		1,600	108	128	136	No	Dyspnea; fatigue; pain
		2,400	116	126	136	No	Dyspnea marked; exhaustion; pain
		1,000	122	122	142	No	
		*(10 s.20) 2,100	114	122	134	No	Dyspnea marked; exhaustion; pain
		1,200	110	130	134	No	
		1,600	112	126	136	No	
		(10 s.25) 3,000	114	130	130	No	Dyspnea marked; exhaustion; pain
S. R. 21	Severe	2,000	130	126	140	No	
		3,000	122	118	152	No	Dyspnea and fatigue
		(20 s.20) 4,000	124	116	130	No	Dyspnea; fatigue; pain
		1,000	126	114	142	No	
		2,000	136	126	140	No	Dyspnea; fatigue
		2,400	126	124	126	No	Dyspnea marked; exhaustion; pain
		2,100	110	112	126	No	
		3,000	112	112	124	No	
		(20 s.20) 4,000	110	106	114	No	Dyspnea marked; fatigue; pain
P. R. 23	Severe	2,000	144	146	156	No	
		(20 s.15) 3,000	142	142	152	No	Dyspnea; fatigue; pain; palpitation
		2,000	140	144	152	No	
		3,000	134	138	152	No	Dyspnea marked; fatigue; pain
S. B. 23	Severe	2,300	122	132	156	No	
		3,400	120	130	148	Yes	Dyspnea; fatigue
		2,300	130	142	162	No	
		3,400	130	138	160	Yes	Dyspnea; fatigue
		(20 s.20) 4,000	122	128	154	Yes	Dyspnea marked; exhaustion
A. V. 28	Severe	2,300	124	144	144	No	
		3,400	122	134	134	No	Marked dyspnea and fatigue
		(20 s.20) 4,500	116	134	134	No	Marked dyspnea; exhaustion
		2,300	116	142	142	No	
		3,400	120	136	142	Yes	Marked dyspnea and fatigue
		2,300	118	144	144	No	
		3,400	114	140	152	Yes	Marked dyspnea and fatigue
		4,600	112	124	140	No	6 wks. since 1st observation; daily exercise since
		6,900	106	112	142	No	Dyspnea and fatigue
		7,900	102	118	136	No	Dyspnea marked; exhaustion
		6,600	106	118	140	No	
		7,100	106	124	134	No	2 mos. since 1st observation; daily exercise since
		9,200	102	122	133	No	Dyspnea marked; fatigue
K. X. 27	Moderate	3,700	152	156	178	No	
		5,000	146	154	168	No	
		(25 s.20) 5,500	156	152	156	No	Dyspnea marked; fatigue; pain
		4,000	148	166	168	No	
		5,900	149	160	168	No	
		(25 s.25) 7,000	142	154	160	No	Dyspnea marked; exhaustion; pain

* "10 s.20" signifies a 10-pound bell swung 20 times.

TABLE 2.—Reactions of Systolic Blood Pressure to Graduated Work in Cases of Tachycardia—(*Continued*)

Name and Age	Type of Case	Work in Foot-Pounds	Systolic Blood Pressure				Remarks
			Before Work	After Work			
				First Reading	Maximum Reading	Delayed Rise	
C. G. 22	Moder-	3,100	130	134	156	No	
		4,000	122	128	160	No	
		(20 s.25) 5,000	122	138	162	No	Marked dyspnea and exhaustion
A. S. 22	Mild	6,300	124	150	170	No	
		9,400	124	141	158	No	
		10,600	122	130	156	No	Dyspnea and fatigue
		6,300	132	166	182	No	
		9,400	134	164	170	No	
		11,000	134	152	162	No	Dyspnea marked; fatigue
S. P. 22	Mild	5,600	126	144	172	No	
		6,700	122	142	162	No	Dyspnea marked and fatigue
		5,100	140	158	178	No	
		7,700	134	154	180	No	Dyspnea marked; exhaustion
		5,100	134	132	176	No	Dyspnea marked and fatigue
		6,100	132	138	174	No	Dyspnea marked and fatigue
W. R. 25	Mild	3,000	148	160	182	No	
		5,400	148	164	182	Yes	
		6,700	146	168	182	Yes	Dyspnea; fatigue; palpitation
		7,000	146	154	180	No	Dyspnea; exhaustion; palpitation
		5,400	146	156	172	No	
		6,700	136	148	178	No	
		7,000	134	152	182	No	Dyspnea; fatigue; palpitation
P. R. 23	Mild	7,500	148	158	176	Yes	
		8,700	142	144	158	Yes	Dyspnea and fatigue
		10,000	138	144	156	No	Dyspnea marked and fatigue
		6,000	148	154	162	No	
		7,500	146	154	162	No	
		9,000	136	146	152	No	Dyspnea and fatigue
R. D. L. 26	Mild	5,300	114	120	132	No	
		6,600	114	116	124	No	Dyspnea; fatigue
		7,000	108	120	128	No	
		9,000	104	100	122	No	Dyspnea; fatigue
		9,300	110	100	119	No	Dyspnea marked; fatigue
F. M. 22	Mild	4,700	128	136	142	No	
		6,900	128	142	156	No	
		9,300	128	138	156	Yes	Dyspnea marked; fatigue; vertigo
		4,700	130	142	166	No	
		6,900	132	144	166		
		9,300	116	132	156	Yes	Dyspnea marked; fatigue
L. H. 22	Mild	5,300	142	152	172	No	
		6,600	140	156	176	No	
		7,900	134	150	181	Yes	Dyspnea and exhaustion

do normal men after the same quantities of work.[1] The pulse rate failed to return to normal inside of 120 seconds in sixteen instances when the heart was overtaxed; five times it returned to normal inside of 120 seconds, although the heart was evidently overtaxed; on nine occasions it failed to return to normal inside of 120 seconds, although the heart was *not* overtaxed.

The curve of the systolic blood pressure showed several interesting anomalies when compared with the curves of normal individuals. "A delayed rise" in pressure ("delayed summit," Cotton, Rapport and Lewis[2]) following heavy work is an almost invariable finding in normal persons. In these persons, both of the severe and mild types, it is seldom found, and when present does not persist as in normal people.

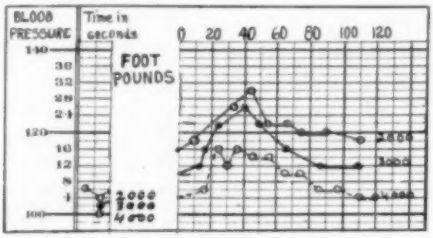


Chart 1.—Blood pressure curves ("diminuendo" type) following increasing amounts of work in S. R., a severe form of case.

The great majority of these patients, both severe and mild, also show blood pressure curves following increasing amounts of work of what may be called a "diminuendo" type. The curves, instead of mounting higher and higher as they do in normal persons after increasing quantities of work, fall lower and lower. The smallest amount of work was followed by the highest curve and the greatest amount by the lowest curve. Charts 1 and 2 exemplify these peculiarities. We have observed this type of curve occasionally in cases of cardiac insufficiency after increasing amounts of work.

The various reactions to work which we have described make it evident that, whatever the underlying cause of the circulatory condition in this small group of men may be, the heart's reserve power in each one was decreased.

One man (A. V.) was given daily graduated exercises with dumbbells and the excellent effect on the cardiac reserve power may be seen in Table 2.

These severe cases resemble closely those described by Lewis and his associates as suffering from "disordered action of the heart."

2. Cotton, Rapport and Lewis: Heart, 1917, **6**, 269.

Mild Type.—There were nine patients who were placed in this class chiefly because of their ability to perform amounts of work approximately normal without evidencing the symptoms of distress exhibited by the former group. Several of these mild cases (K. X. and C. C.) were on the borderland between severe and mild, one of the patients having precordial pain after fairly heavy amounts of work.

The pulse rates were all above normal. Immediately after work they were occasionally higher than those of normal men after similar quantities of work; nineteen times when the heart was evidently overtaxed the pulse rate failed to return to normal inside of 120 seconds; three times the pulse rate *did* return to normal inside of 120 seconds, although the heart was overtaxed; sixteen times the pulse rate failed to return to normal inside of two minutes, although the work had *not* overtaxed the heart.

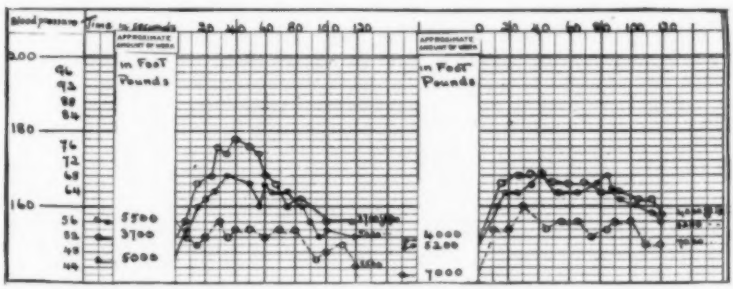


Chart 2.—Blood pressure curves ("diminuendo" type) following increasing amounts of work in K. X., a case of moderate severity.

The curve of the systolic blood pressure showed more frequently a "delayed rise" after heavy work than did the preceding group of severe types, but it was quite inconstant.

The curves of the pressure following increasing amounts of work frequently showed the "diminuendo" type referred to above.

In these mild types of cases the patients were apparently able to do, without undue distress, about as much work as normal men. The only variations from normal which they showed were the tachycardia, the infrequent presence of a delayed rise in the systolic blood pressure curve, and the frequent presence of a "diminuendo" type of curve.

SUMMARY

The reactions to work of fourteen men with tachycardia, between the ages of 21 and 30, were observed on a number of occasions.

Five men were classified as belonging to a severe type, chiefly because of their inability to perform amounts of work which normal

men are capable of and because the performance of comparatively small amounts of work was accompanied by signs of distress — dyspnea, exhaustion or precordial pain.

Reaction of the pulse rates and systolic blood pressure curve to graduated work and their deviations from normal have been described.

21 West Eighty-Fourth Street.

THE EFFECT OF THYMUS GLAND INJECTION ON THE GROWTH AND BEHAVIOR OF THE GUINEA-PIG

AN EXPERIMENTAL INVESTIGATION *

D. M. OLKON, M.D.
CHICAGO

The functions of the endocrine organs have been investigated, for the most part, by three methods, namely, by extirpation of the gland, by feeding normal animals the dried gland or its extracts, and, finally, by the injection into the blood stream or the peritoneal cavity of solutions prepared from the organs. Morphologic studies of these tissues, directed mainly towards discovering evidence of secretory activity, have yielded confirmatory results in some cases, although it must be admitted that the chief effects of these organs are physiologic in nature, affecting metabolism and function in certain ways. Gradually our knowledge of the specific activities of the thyroid gland, the adrenals and the hypophysis, has been becoming exact and definite. The status of our knowledge of the endocrine functions of certain other structures such as the testes, ovary and corpus luteum is not so satisfactory. We are far from possessing any certain conclusive information with regard to the specific hormones of these organs. The thymus gland is likewise a *terra incognita* in spite of the numerous studies which have been made of it during the past few years. In the hope of adding something to our knowledge of this organ, the experiments which form the body of this paper were undertaken.

A review of the literature, a summary of which is given later in this article, shows that the results of previous investigations are far from concordant and mutually confirmatory. Many of the discrepancies are doubtless due to the fact that many different species of animals, standing far apart in the animal scale, have been used for thymus gland experiments. Thus, in the feeding experiments, Abderhalden and Bartlemez used frogs, Gudernatsch used tadpoles, Hoskins albino rats, Klose and Vogt dogs, Paton guinea-pigs. But even where the animals were closely related, the results of much of this work are directly contradictory. Hewer found that thymus gland feeding retarded the development of the testes of young white rats and also

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* From the Psychopathic Laboratory of the University of Chicago, under the direction of Dr. H. C. Stevens.

TABLE 1.—Tabular Review of the Literature. The Results of Extirpation Experiments

Author	Publication	Date	Animal Used	Results
1. Abelous and Billard	Arch. de physiol.	1896	Rabbits, frogs	Great muscular weakness. Death in three to fourteen days in frogs. In rabbits there were symptoms of intoxication followed by stupor.
2.			Dogs	Softening of the bones with increased excretion of calcium salts. Fractures tended to heal badly, and with less callus; the bones tended to bend.
3. Basch, K.	Jahrb. f. Kinderh.	1906	Puppies	Muscular weakness and a diminution of intelligence. The puppies became sluggish and lost in weight; finally they became very stupid.
4. Basch, K.	Ibid.	1908	Dogs	Bones became soft. The excitability of the peripheral nervous system was markedly increased; muscular tremor very pronounced. The animals lost in weight, although they continued to eat enormously. They finally died.
5. Biedl, A.	Wien. Klin.	1903	Hens	Weakness of the legs, tremor of the entire body, and finally death.
6. Biedl, A.	Ibid.	1903	Birds	No observable symptoms.
7. Brocci, C.	Rev. di clin. pediat.	1905	Rabbits	Reduction of calcium in the bones.
8. Colzolari, A.	Arch. ital. di biol.	1898	Rabbits	Castration increased the weight of the thymus gland
9. Fischl, Z.	Ztschr. f. Exper. Path. u. Therap.	1905	Rabbits, goats, dogs	Negative symptoms
10. Ghika, C.	Thèse de Paris	1901	Guinea-pigs, rabbits	Castration caused persistent growth of the body, and retarded atrophy of the thymus gland
11. Goodall and Paton	Jour. Physiol.	1904	Guinea-pigs	There was a diminution of the number of leukocytes, but no apparent change in the rate of growth of the animal
12. Gebele and Miss Hewer	Ztschr. f. exper. Path.	1910	Dogs	Muscular weakness. No other changes
14. Henderson, J.	Jour. Physiol.	1904	Rabbits, guinea-pigs, bulls, heifers	Castration in guinea-pigs, rabbits, and cattle caused a persistent growth and a retarded atrophy of the thymus gland. In bulls and unspayed heifers normal atrophy of the thymus was greatly accelerated
15. Hammar, J A.	Arch. f. d. ges. Physiol.	1907	Frogs	No symptoms
16. Hart and Nordman	Berl. klin. Wchnschr.	1910	Dogs	Muscular weakness. No other death
17. Kloss and Vogt	Centrabl. f. Med. u. Chir.	1909	Dogs	Muscular weakness. Death eventually occurred from its removal
19. Paton, D. Noel	Jour. Physiol.	1908	Guinea-pigs	Castration before sexual maturity was followed by an increase in size of the thymus, and involution of the gland was retarded

TABLE 1.—Tabular Review of the Literature. The Results of Extirpation Experiments—(*Continued*)

Author	Publication	Date	Animal Used	Results
20. Paton, D. Noel	Jour. Physiol.	1905	Guinea-pigs	The removal of the thymus gave rise to a more rapid growth of the testes, but no apparent influence on the general growth of the animal
21. Ranzi and Tandler	Wien. klin. Wchnschr.	1909	Dogs	Emaciation. The bones became soft and bent easily
22. Sommer and Florcken	Med. Ges. zu Wurzb.	1908	Dogs cats	Animals were awkward in shape and clumsy; their hair became coarse, their coats rough, and their general behavior stupid
23. Soli, U.	Presse Méd.	1907	Hens, capons	Laid eggs without shells. Removal of the thymus produced a reduction in the weight of the testicles
24. Taruli and Lo Monaco	Bull. accad. med. di Roma	1897	Dogs	In only the very young puppies had extirpation any results. There were in these cases disturbances of nutrition, diminished muscular power, diminution of the red blood corpuscles and of the hemoglobin. The disturbances disappeared when the dogs grew older
25. Vincent, S.	Jour. Anat. and Physiol.	1903	Frogs	No bodily changes
26. Vincent, S.	Proc. Phy. Soc. Jour. Physiol.	1904	Guinea-pigs	No symptoms of any kind

caused degeneration in the testes of adult male rats. Hoskins found that feeding albino rats with thymus gland produced no constant effect on the body as a whole or of any particular organs. Paton, employing the same method with guinea-pigs, reported that the growth of the testes was more rapid. Here, in the study of one specific question, namely, the influence of the thymus gland on the testes, one receives three different answers. The method of extirpation has not been more successful than that of feeding. One reason for this lies in the structure of the thymus gland, in certain forms at least. In the guinea-pig, as Park has recently shown, small masses of thymus tissue are scattered about in the neck adjacent to the main seat of this gland. Obviously, extirpation, under these conditions, can never be complete. The two results which stand out most conspicuously in the extirpation experiments are changes in calcium metabolism and evidence of a reciprocal relation between thymus and testes. With the method of injection, investigators have been concerned for the most part with the immediate results of the injection. They report a fall in blood pressure, acceleration of pulse, dyspnea and diarrhea. In no case, however, have prolonged studies been made by this method. It had seemed to us, therefore, that because of the possibility of incomplete

extirpation and because of the difficulty of causing certain species to feed on thymus gland, the injection method was the method of choice for an experimental attack on this problem. By means of this method one can control absolutely the size and frequency of the dose. Furthermore, we have chosen to determine the effect of this gland on the general metabolism of the guinea-pig as measured by growth of males. A subsidiary problem, namely, the effect of thymus gland injections on the growth of young females, was also studied. The latter results have some bearing on the question of the reciprocal relation between thymus and testes which appears as a result of castration.

TABLE 2—LITERATURE ON THE RESULTS OF FEEDING EXPERIMENTS

Author	Publication	Date	Animal Used	Results
1. Abderhalden, E.	Arch. d. ges. Physiol.	1915	Frogs	Darker skin; very active; retarded metamorphosis
2. Bartelmez, B. W.	Anat. Record (Proceedings)	1915	Amblystoma, Tigrinum Rana Catesbiana	In Rana it caused more rapid development. Amblystoma metamorphosed normally, but sooner
3. Güdernatsch, J. F.	Am. Jour. Anat.	1913	Toads	Stimulated body growth, but inhibited metamorphosis of limbs and tail; hence it has the power to suppress differentiation. They were very active in their movements as contrasted with other feedings
4. Güdernatsch, J. F.	Arch. f. Entwekings-mechn.	1912	Tadpoles	Thymus feeding gave rise to dark colored skin. A good many died early, presenting a "status thymicus." Growth of body was greatly increased
5. Hoskins, E. R.	Jour. Exper. Zoöl.	1916	Albino rat	The results were negative, with no marked constant effect on the body as a whole or on any particular organ. Microscopic examination of the testes showed no degeneration. The apparent decrease in the weight of the male spleen is doubtful
6. Hewer, E. E.	Jour. Physiol.	1916	White rat	Retarded the development of the testes in the young rats and caused degeneration of the testes in the adults
7. Hewer, E. E.	.....	1916	White rat	Reduced the development of the testes in the young males
8. Klose and Vogt	Klin. u. Biol. der Thymusdruse	1910	Dogs	Produced diarrhea
9. Paton, D. N.	Jour. Physiol.	1904	Guinea-pigs	The growth of the testes was more rapid
10. Romeis, B.	Arch. f. Entwekings-mechn.	1915	Frogs	Increased body growth considerably, but retarded metamorphosis
11. Salkind, J.	Arch. d. Zoöl. exper. et gén.	1915	Dogs	Stimulated general growth from a large amount of feeding of thymus gland

General Conditions of the Experiments.—Armour's preparation of the thymus gland of the sheep was used. The powdered gland was triturated in sterile physiologic salt solution until a uniform suspension was obtained. The initial dose was 1 grain of the dried gland for four weeks. The dosage was increased half a grain every two weeks for six weeks. It was then increased every week for three weeks. During the last two weeks of the experiment the dose was increased twice each week. In no case, however, did the maximal dose exceed 10 grains for each injection. The injection was made with a sterilized needle and syringe into the peritoneal cavity. Each animal used in the experiments was injected twice a week and weighed once a week.

TABLE 3.—THE RESULTS OF INJECTION EXPERIMENTS

Author	Publication	Date	Animal Used	Results
1. Abderhalden, E.	Ztschr. f. physiol. Chem.	1912	Dogs	Repeated injections into the peritoneal cavity produced a fall in blood pressure, dyspnea, cramp of unstriped muscle and diarrhea
2. Basch, K.	Ztschr. f. Path. u. Therap.	1913	Dogs	Injections of extracts into the blood stream caused a marked fall of blood pressure
3. Bickel, A.	Med. Wchnschr. Berl.	1901	.....	Fall of blood pressure
4. Gebele	Beitr. z. klin. Chirurg.	1910	Dogs	Enlargement of the testicles. No increase of body growth
5. Popper, R.	Sitzung. d. k. Akad. zu Wien.	1905 1906	Dogs, rabbit	Reduction of arterial tension and dyspnea
6. Patton and Goodall	Proc. Royal Soc. Edinb.	1905	Guinea-pigs	Caused lowered blood pressure with symptoms of suffocation
7. Svehla, K.	Wien. med. Wchnschr.	1906	Dogs	Produced acceleration of the pulse and a marked reduction of arterial tension
8. Vincent, S.	Proc. Physiol. Soc. London	1904	Frogs	No observable symptoms
9. Vincent and Sheen	Jour. Anat. and Physiol.	1904	Guinea-pigs	Acceleration of the pulse and a fall of blood pressure
10. Svehla, K.	Arch. f. exper. Path. u. Pharmakol.	1900	Infants	No definite symptoms

To study the effect of thymus gland injection on growth, eight male guinea-pigs of approximately the same age and weight were chosen. Two of these animals were treated with thymus gland; two received a suspension of sheep muscle; two received injections of tenth-normal sodium chlorid solution and two were used as normal controls. To study the influence of sex on thymus gland injections, a series of four female guinea-pigs of the same litter were taken when 15 days old. Two of these animals were given thymus gland injections and two were used as normal controls. The injections of sheep muscle were made in order to have a control on the effect of the injection of sheep protein. By comparing the growth curves of these animals which received the muscle with similar curves for the thymus pigs, the specific effect of the thymus is apparent; the salt solution injections were deemed advisable in order to have a control on the effect on growth of repeated punctures of the abdominal wall and injections of foreign substances into the peritoneal cavity. The growth curves of these animals show that the punctures and injections of sodium chlorid retard growth very little.

From the foregoing data it seems reasonably safe to assume that the thymus gland is in some way responsible for disturbances of growth and development, and, moreover, the evidence thus far produced is also partly in favor of the assumption that the thymus and the lymphatic system are coordinated in function and that the thymus itself is probably concerned with the development of the sexual glands. This does not necessarily mean, however, that the thymus itself is an independent organ, but that it has a general influence in the chemistry of the ductless glands and also in a specific way by itself. Some notable investigators have also shown that a thymus hyperplasia produces a change in the circulation of the thymus which not infrequently is accompanied by sudden death. The thymus gland has also been regarded as a blood-forming organ, and Schaffer[1] is the most recent advocate of this view. He believes, as a result of his studies on cats and rabbits, that the hemopoietic function is like that of the spleen, liver and bone marrow.

TABLE 4.—Averages of Gain and Loss in Weight of Guinea-Pigs in Grams per Week

Thymus				Muscle			
Guinea-pig I		Guinea-pig II		Guinea-pig I		Guinea-pig II	
Initial Weight, Gm.	+ = Gain − = Loss in Gm.	Initial Weight, Gm.	+ = Gain − = Loss in Gm.	Initial Weight, Gm.	+ = Gain − = Loss in Gm.	Initial Weight, Gm.	+ = Gain − = Loss in Gm.
208		284		365		385	
292	+24	285	+1	379	+14	305	−29
301	+33	239	+45	377	+12	421	+36
328	+60	331	+47	402	+37	416	+31
298	+30	391	+107	362	−3	395	+10
	Av. +29 2/5		Av. +22		Av. +12		Av. +10
664		624		321		372	
660	−4	638	+14	385	+64	450	+78
653	−11	641	+17	405	+84	489	+117
633	−31	583	−41	417	+96	482	+110
613	−51	587	−37	421	+100	496	+124
617	−47	602	−22	416	+95	468	+96
625	−39	587	−37	433	+112	521	+149
576	−88	541	−83	455	+134	523	+151
608	−56	546	−78	451	+130	538	+166
640	−24	488	−136	452	+131	445	+73
635	−29	536	−88	462	+141	546	+174
	Av. −34 6/11		Av. −44 7/11		Av. +98 9/11		Av. +112 6/11

1. The references will be found arranged alphabetically at the end of the article.

TABLE 5.—Table of Averages

Tenth-Normal NaCl Solution				Controls			
Guinea-pig I		Guinea-pig II		Guinea-pig I		Guinea-pig II	
Initial Weight, Gm.	+ = Gain − = Loss in Gm.	Initial Weight, Gm.	+ = Gain − = Loss in Gm.	Initial Weight, Gm.	+ = Gain − = Loss in Gm.	Initial Weight, Gm.	+ = Gain − = Loss in Gm.
452		481		440		402	
478	+26	517	+36	478	+38	426	+24
488	+36	507	+26	496	+56	460	+58
425	−37	550	+69	533	+93	504	+102
552	+100	567	+86	561	+121	419	+17
468	+16	515	+34	482	+42		
475	+23	487	+6	511	+71	453	+51
532	+80	506	+25	575	+135	541	+139
577	+125	516	+35	646	+206	593	+161
552	+100	565	+84	623	+183	551	+149
589	+137	605	+124	660	+220	577	+175
631	+179	626	+145	698	+258	580	+178
650	+198	655	+174	701	+261	638	+236
678	+226	609	+188	741	+301	670	+268
672	+220	724	+243	789	+349	688	+286
688	+236	738	+257	755	+315	655	+253
	Av. +104 11/16		Av. +95 1/8		Av. +165 9/16		Av. +139 4/5

TABLE 6.—Table of Averages

Thymus				Controls			
Guinea-pig I		Guinea-pig II		Guinea-pig I		Guinea-pig II	
Initial Weight, Gm.	+ = Gain − = Loss in Gm.	Initial Weight, Gm.	+ = Gain − = Loss in Gm.	Initial Weight, Gm.	+ = Gain − = Loss in Gm.	Initial Weight, Gm.	+ = Gain − = Loss in Gm.
100		96		97		89	
116	+16	91	−5	93	−4	92	+3
116	+16	93	−3	110	+13	84	−5
104	+4	104	+8	96	−1	105	+16
124	+24	123	+27	109	+12	123	+34
137	+37	125	+29	138	+41	178	+89
152	+52	142	+46	173	+76	215	+126
169	+69	170	+74	196	+99	239	+150
194	+94	165	+69	230	+133	275	+186
219	+119	187	+91	257	+160	316	+227
237	+137	206	+110	281	+184	340	+251
231	+131	221	+125	327	+230	381	+292
258	+158	249	+153	359	+262	383	+294
	Av. +65 12/13		Av. +55 9/13		Av. +92 9/13		Av. +127 12/13

THE EXPERIMENT

Material.—April 17, 1917, eight male guinea-pigs of approximately the same size were selected. Each animal was carefully marked and a record of the markings kept. They were paired off as to size and weight and their general behavior noted. Two of the guinea-pigs were used for thymus injection, two for the muscle injections, two for decinormal sodium chlorid injection and two acted as normal controls.

A second series of guinea-pigs, four in number and all females from the same litter, were taken on May 8, when only 15 days old. Two of them were given thymus injections and two were used as controls. This was done to ascertain the difference in effect of thymus injection between the male and female guinea-pigs.

TABLE 7.—TABLE OF AVERAGES

Guinea-pig I		Guinea-pig II	
Initial Weight, Gm.	+ = Gain; − = Loss in Gm.	Initial Weight, Gm.	+ = Gain; − = Loss in Gm.
785		727	
672	−113	666	−61
735	−50	723	+4
720	−65	611	−116
676	−109	590	−128
682	−103	646	−81
	Av. −73 1/3	604	−123
657		622	−105
637	−20	621	−106
650	−7	622	−105
598	−59	631	−96
628	−29		
661	+4	675	−52
	Av. −18 1/3		Av. −80 9/12

Interval of Injections.—The injections were given twice a week, starting with 1 grain of the powdered gland (Armour). The dose was increased a half grain every fortnight at first, then every week; in the last two weeks of the experiment the dose was increased 1 grain twice each week. An exception was made when the quantity reached 3.5 grains per injection; this dose was kept up for four injections.

The Weighing.—The animals were weighed once a week before the injection was given and before they were fed.

The materials for injection used were:

1. Desiccated powdered sheep's muscle.
2. Desiccated powdered sheep's thymus gland.
3. Decinormal sodium chlorid solution.

A summary of loss and gain of body weight in grams per week was as shown in Table 4.

COMMENT AND CONCLUSIONS

Our investigation on the effect of thymus injection on the growth and behavior of the guinea-pig made prominent several features: (1) that protein injections give rise to metabolic disturbances, evidenced by the change in rate of growth and in the general bodily signs and symptoms; (2) that more noticeable changes occurred when thymus was injected.

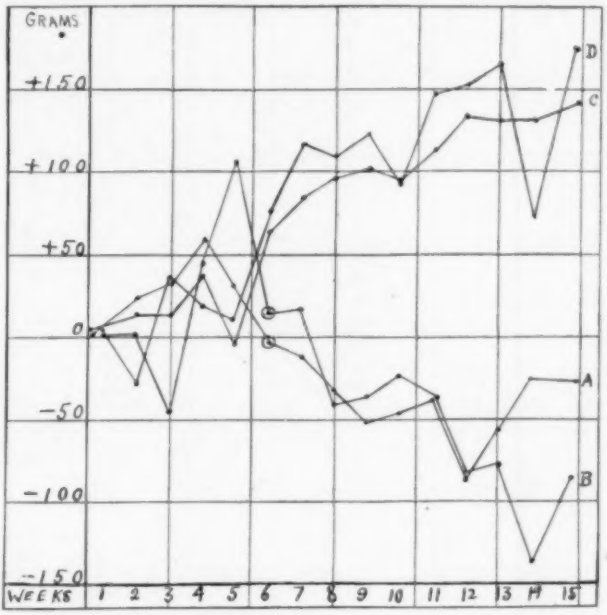

Chart 1.—Series I and Series II. Comparison of deviations of body weight per week; + = gain; — = loss in grams; A = thymus-injected Guinea-Pig I; B = thymus-injected Guinea-Pig II; C = muscle-injected Guinea-Pig I; D = muscle-injected Guinea-Pig II; all males; ⊙ = new guinea-pig.

Weintraub and Mayer have shown that thymus feeding causes a striking increase in the output of uric acid. The experiments of Thirloix, Bernard, Abelous, and Billard show that the removal of the thymus in rabbits and frogs gives rise to symptoms of intoxication, proving fatal. When half of the organ is removed, death of the animal does not occur, but the remaining half of the gland becomes hypertrophic. These results suggest that, besides any routine function the thymus may have as lymphatic tissue, it has some more specific effect on the life of certain animals. Basch, König and Tandler, Klose and Vogt found that the removal of the thymus in dogs causes an

increased excretion of lime salts and a deficient ossification of the bones; and in some instances it was followed by coma and death. Svehla's injection of thymus in dogs gave rise to a quickened pulse rate and a fall of blood pressure and dyspnea. Paton and Goodall found that injections of extracts of thymus in guinea-pigs caused a lowering of blood pressure, cardiac weakness, dyspnea, and finally death. Paton's and Henderson's experiments show that there is a reciprocal action between the thymus and testes, each checking the

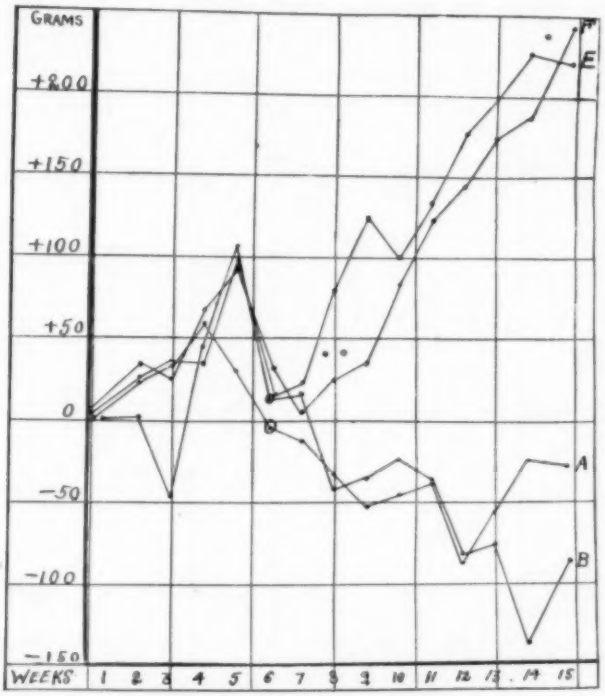

Chart 2.—Series I and Series III. Comparison of deviations of body weight per week; + = gain; — = loss in grams; A = thymus-injected Guinea-Pig I; B = thymus-injected Guinea-Pig II; E = tenth-normal sodium chlorid solution injected Guinea-Pig I; F = tenth-normal sodium chlorid solution injected Guinea-Pig II; all males; ⊙ = new guinea-pig.

growth of the other. Castration delays involution of the thymus, while removal of the thymus causes a more rapid development of the testes. Various other investigators, such as Ghika, Gudernatsch, Romeis and Bartelmez, found that the thymus possesses vegetative functions, for the feeding of thymus gave rise to larger-sized bodies, but arrested metamorphosis. Soli, Henderson, Gebele, Hewer and

Hoskins have shown that thymus extirpation, thymus irradiation and thymus feeding inhibited the maturity of the sexual glands. As has been said before, another function attributed to the thymus is that of a blood-forming organ.

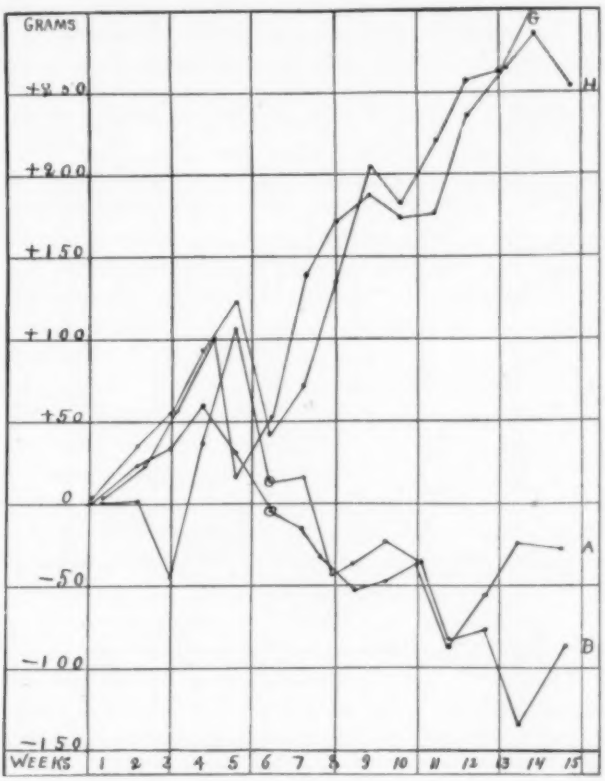

Chart 3.—Series I and Seriess IV. Comparison of deviations of body weight per week; + = gain; — = loss in grams; A = thymus-injected Guinea-Pig I; B = thymus-injected Guinea-Pig II; G = control Guinea-Pig I; H = control Guinea-Pig II; all males; ⊙ = new guinea-pig.

This experiment brought out the fact that when the additional thymus as injected, a change in the body economy took place. This struggle between the animal and the invading protein represents a situation in which disorganization had taken place, and the conflict resulted in a general body loss and in deranged behavior which was made manifest in the symptomatic signs and symptoms.

The significance of this experiment is the evidence it gives of the specific changes caused by the injection of proteins. Among the many and varied signs and symptoms observed after injection were: contraction of limbs, contraction of the large trunk muscles; spasms of smaller muscle groups about face and neck; undue bodily movements; overexcitability when the dose injected was comparatively small (1 or 2 grains); sluggishness and extreme cessation of action simulating depression when large doses were given. Another feature was that

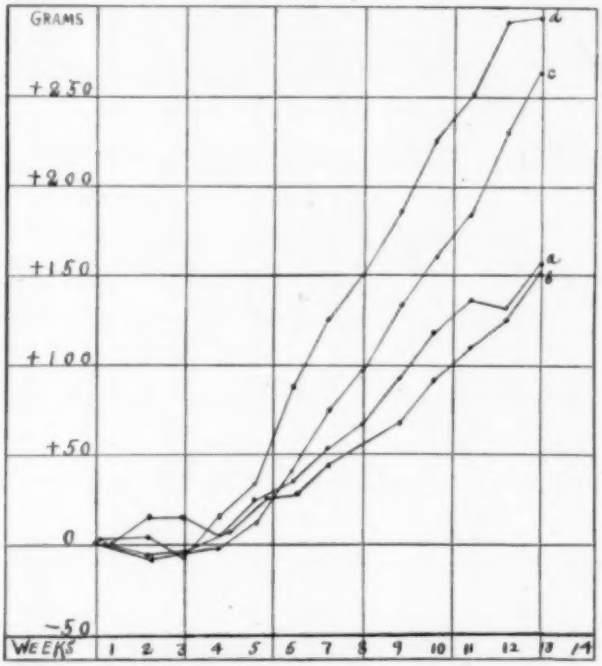

Chart 4.—Series V. Comparison of deviations in body weight per week; + = gain; — = loss in grams; a = thymus injected Guinea-Pig I; b = thymus-injected Guinea-Pig II; c = control Guinea-Pig I; d = control Guinea-Pig II; all very young females.

the hair became dry and rough, and the animals looked emaciated. Dyspnea and convulsions were the outstanding phenomena in the thymus series. In one instance death followed the extreme dyspnea after 4 grains were injected. In two other instances the animals died the afternoon of the day of injection.

These marked effects after thymus injection as compared with the other mediums of the experiment, namely, that of muscle and of

tenth-normal salt solution, call for interpretation of the differences as well of the likeness in the behavior of the guinea-pig. It might be argued that such manifestations in the behavior of the guinea-pig as contraction of limbs, spasms, unrest, excitability, sluggishness, cramps, convulsions, dyspnea and the like, are not measureable entities and therefore ought to be left out in the assignment of a causal connection between thymus injection and behavior. Yet one is scarcely justified in nullifying all such phenomena. When we consider the signs and symptoms that follow the injection of thymus, and compare these animals with those receiving injections of muscle, of sodium chlorid solution, and again with the control animals, it becomes apparent how much more acute and representative are the signs and symptoms that follow thymus injection.

In the case in which a necropsy was had soon after the guinea-pig succumbed to the injection, the blood in the heart and large vessels was found clotted. This finding coincides with the findings of Popper, who says that thymus injected intravenously gave rise to clotting of blood in the vessels. Of course, the clotting might have been produced in the blood stream either from indirected pressure or from substances thrown into the circulation which affect the circulatory or respiratory centers; but this does not eliminate the probability of toxins in the blood stream, as well as a specific entity that plays the rôle of disorganizer, namely, thymus specificity.

The results of our experiment put it within the limits of probability that the thymus gland, whatever its proteolytic rôle common to all animal proteins may be, has a more specific property, namely, that of influencing the bodily growth and behavior of the guinea-pig.

Additional work is necessary also to establish the causal connection between the thymus and its specificity as the gland of internal secretion that regulates growth of the sexual glands and the disorganization of bony structure.

SUMMARY

Since our investigation is of small magnitude, we are justified in drawing conclusions only in so far as our evidence will permit. The most striking and outstanding features are as follows:

1. Reduction of weight in the male guinea-pig was produced experimentally by the injection of thymus gland intraperitoneally.

2. After the injection, well-marked changes took place, namely, muscle spasm, dyspnea, and convulsion.

3. The muscular spasms that occurred after thymus was injected appeared more severe and of longer duration than of either the muscle or of the tenth-normal sodium chlorid injected guinea-pigs.

4. Some animals died after large doses of thymus injection.

5. The general appearance of the animals in the thymus series was that of grave metabolic disturbances, emaciation, accompanied by dryness and roughness of their fur.

31 North State Street.

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